	Issue Date	Pages	Document ID	Title
1	20030313	222	US 20030050230 A1	STE20-RELATED PROTEIN KINASES
2	20021114	345	US 20020168711 A1	Nucleic acids, proteins, and antibodies
3	20030429	56	US 6555547 B1	Method for treating a patient with neoplasia by treatment with a vinca alkaloid derivative
4	20030415	38	US 6548602 B2	Polymeric film compositions having controlled viscosity response to temperature and shear
5	20011106	102	US 6312934 B1	Human MEKK proteins, corresponding nucleic acid molecules, and uses therefor
6	20001226	53	US 6165461 A	Tao protein kinases and methods of use therefor
7	19960910	19	US 5554664 A	Energy-activatable salts with fluorocarbon anions

	L #	Hits	Search Text
1	L1	5951	TAO$2
2	L2	11008	mek$2
3	L3	7	l1 same l2
4	L4	832317	activat$3 or modulat$3
5	L5	3	l3 same l4
6	L6	174	"atf2"
7	L7	1	l1 same l6
8	L8	1472	"p38"
9	L9	3	l1 same l8
10	L10	653	cobb.in.
11	L11	2	l1 and l10
12	L12	21587	chen.in.

	L #	Hits	Search Text
13	L13	395	l1 and l12
14	L14	1	l3 and l12
15	L15	611	berman.in.
16	L16	1	l1 and l15
17	L17	552	hutchison.in.
18	L18	1	l3 and l17

	Issue Date	Pages	Document ID	Title
1	20010515	8	US 6232427 B1	Esterification method
2	20001226	53	US 6165461 A	Tao protein kinases and methods of use therefor

	Issue Date	Pages	Document ID	Title
1	20030313	222	US 20030050230 A1	STE20-RELATED PROTEIN KINASES
2	20021114	345	US 20020168711 A1	Nucleic acids, proteins, and antibodies
3	20001226	53	US 6165461 A	Tao protein kinases and methods of use therefor

	Issue Date	Pages	Document ID	Title
1	20030313	222	US 20030050230 A1	STE20-RELATED PROTEIN KINASES
2	20020221	34	US 20020022032 A1	Immuno-adjuvant PDT treatment of metastatic tumors
3	20001226	53	US 6165461 A	Tao protein kinases and methods of use therefor

=> d his

(FILE 'HOME' ENTERED AT 10:36:41 ON 16 MAY 2003)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:39:00 ON 16 MAY 2003

```
L1          5251 S TAO##
L2         39224 S MEK##
L3            29 S L1 AND L2
L4             9 DUP REM L3 (20 DUPLICATES REMOVED)
L5       4622124 S MODULAT? OR ACTIVAT?
L6         30356 S P38
L7          1054 S ATF2
L8            13 S L1 AND L6
L9             5 DUP REM L8 (8 DUPLICATES REMOVED)
L10         4232 S L2 AND L6
L11         4154 S L10 AND L5
L12           68 S  L11 AND L7
L13           20 DUP REM L12 (48 DUPLICATES REMOVED)
                 E COBB M H/AU
L14          572 S E3
L15           15 S L1 AND L14
L16            5 DUP REM L15 (10 DUPLICATES REMOVED)
                 E HUTCHISON M/AU
L17          158 S E3
                 E CHEN Z/AU
L18         6923 S E3
                 E BERMAN K S/AU
L19           24 S E3
L20         7093 S L17-L19
L21           15 S L1 AND L20
L22            5 DUP REM L21 (10 DUPLICATES REMOVED)
```

=>

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1652MXM

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT

MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:36:41 ON 16 MAY 2003

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.84 0.84

FILE 'MEDLINE' ENTERED AT 10:39:00 ON 16 MAY 2003

FILE 'EMBASE' ENTERED AT 10:39:00 ON 16 MAY 2003
COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.

FILE 'BIOSIS' ENTERED AT 10:39:00 ON 16 MAY 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'BIOTECHDS' ENTERED AT 10:39:00 ON 16 MAY 2003
COPYRIGHT (C) 2003 THOMSON DERWENT AND INSTITUTE FOR SCIENTIFIC INFORMATION

FILE 'SCISEARCH' ENTERED AT 10:39:00 ON 16 MAY 2003
COPYRIGHT 2003 THOMSON ISI

FILE 'HCAPLUS' ENTERED AT 10:39:00 ON 16 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'NTIS' ENTERED AT 10:39:00 ON 16 MAY 2003
Compiled and distributed by the NTIS, U.S. Department of Commerce.
It contains copyrighted material.
All rights reserved. (2003)

FILE 'LIFESCI' ENTERED AT 10:39:00 ON 16 MAY 2003
COPYRIGHT (C) 2003 Cambridge Scientific Abstracts (CSA)

=> s TAO##
L1 5251 TAO##

=> s MEK##
L2 39224 MEK##

=> s l1 and l2
L3 29 L1 AND L2

```
=> dup rem l3
PROCESSING COMPLETED FOR L3
L4             9 DUP REM L3 (20 DUPLICATES REMOVED)

=> d 1-9 ibib ab

L4   ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2003:242515  HCAPLUS
DOCUMENT NUMBER:          138:283071
TITLE:                    Proteome-wide analysis of protein interactions by high
                          throughput mass spectrometry
INVENTOR(S):              Bader, Gary; Climie, Shane; Durocher, Daniel; Figeys,
                          Daniel; Gruhler, Albrecht; Heilbut, Adrian Mark; Ho,
                          Yuen; Moore, Lynda A.; Moran, Michael; Muskat, Brenda;
                          Tyers, Michael
PATENT ASSIGNEE(S):       MDS Proteomics, Inc., Can.; Mount Sinai Hospital and
                          Samuel Lunenfeld Research Institute
SOURCE:                   PCT Int. Appl., 133 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     WO 2003025213      A2   20030327       WO 2002-CA1440    20020923
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  US 2001-323930P  P  20010921
                                        US 2001-341213P  P  20011030
                                        US 2002-345286P  P  20020104
AB   Methods and reagents for high throughput anal. of protein-protein
     interaction networks using high-throughput mass spectrometric protein
     complex identification (HMS-PCI) are described. The method is faster and
     less demanding of time than two-hybrid screening and it is feasible to
     identify directly protein complexes on a proteome-wide scale. The method
     uses proteins labeled with an affinity tag, such as an antigen, as baits
     to capture binding partners. Complexes are purified by means of the
     affinity label and the components rapidly characterized by mass
     spectrometry. Using 10% of predicted yeast proteins as baits, 3,617
     protein interactions covering 25% of the yeast proteome were identified.
     Numerous protein complexes were identified, including many new
     interactions in various signaling pathways and in the DNA damage response.
     Comparison of the HMS-PCI data set with interactions reported in the
     literature revealed an av. threefold higher success rate in detection of
     known complexes compared with large-scale two-hybrid studies. Given the
     high degree of connectivity obsd. in this study, even partial HMS-PCI
     coverage of complex proteomes, including that of humans, should allow
     comprehensive identification of cellular networks.

L4   ANSWER 2 OF 9     MEDLINE                          DUPLICATE 1
```

ACCESSION NUMBER: 2001341539 MEDLINE
DOCUMENT NUMBER: 21238279 PubMed ID: 11279118
TITLE: Regulation of stress-responsive mitogen-activated protein (MAP) kinase pathways by **TAO2**.
AUTHOR: Chen Z; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75390-9041, USA.
CONTRACT NUMBER: GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 May 11) 276 (19) 16070-5.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20030105
Entered Medline: 20010614

AB Previous studies demonstrated that in vitro the protein kinase **TAO2** activates MAP/ERK kinases (**MEKs**) 3, 4, and 6 toward their substrates p38 MAP kinase and c-Jun N-terminal kinase/stress-activated protein kinase (JNK/SAPK). In this study, we examined the ability of **TAO2** to activate stress-sensitive MAP kinase pathways in cells and the relationship between activation of **TAO2** and potential downstream pathways. Over-expression of **TAO2** activated endogenous JNK/SAPK and p38 but not ERK1/2. Cotransfection experiments suggested that **TAO2** selectively activates **MEK3** and **MEK6** but not **MEKs** 1, 4, or 7. Coimmunoprecipitation demonstrated that endogenous **TAO2** specifically associates with **MEK3** and **MEK6** providing one mechanism for preferential recognition of **MEKs** upstream of p38. Sorbitol, and to a lesser extent, sodium chloride, Taxol, and nocodazole increased **TAO2** activity toward itself and kinase-dead **MEKs** 3 and 6. Activation of endogenous **TAO2** during differentiation of C2C12 myoblasts paralleled activation of p38 but not JNK/SAPK, consistent with the idea that **TAO2** is a physiological regulator of p38 under certain circumstances.

L4 ANSWER 3 OF 9 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001687134 MEDLINE
DOCUMENT NUMBER: 21590367 PubMed ID: 11733138
TITLE: kin-18, a C. elegans protein kinase involved in feeding.
AUTHOR: Berman K S; Hutchison M; Avery L; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX, USA.
CONTRACT NUMBER: GM53032 (NIGMS)
HL46154 (NHLBI)
SOURCE: GENE, (2001 Nov 28) 279 (2) 137-47.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011205
Last Updated on STN: 20020125
Entered Medline: 20020122

AB **TAO1** and **TAO2** are recently described protein kinases whose initial characterization has placed them at the mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK) kinase

kinase (**MEKK**) level of stress-responsive MAPK pathways. Because their physiological roles have not been identified, we sought to study their C. elegans homolog to learn more about their functions. kin-18 encodes a previously uncharacterized protein in C. elegans whose catalytic domain shares over 60% identity with **TAO1** and **TAO2**. We demonstrate that KIN-18 is a protein of 120 kDa whose promoter is active in the pharynx and intestine of C. elegans. To learn more about **TAO**/KIN-18 function, we studied how expression of constitutively active forms of **TAO1** or KIN-18 would affect the physiology of intact worms. Strains of C. elegans expressing active forms of **TAO1** or KIN-18 exhibit altered pharyngeal electrophysiology as measured by electropharyngeogram. These worms grow more slowly and lay fewer eggs, phenotypes that could result from reduced feeding. We have also identified a C. elegans gene that encodes a protein kinase similar to mammalian MAPK/ERK Kinase (**MEK**) 4 whose promoter is active in the pharynx. It is phosphorylated by **TAO1** in vitro and physically interacts with **TAO1**.

L4 ANSWER 4 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:285372 BIOSIS
DOCUMENT NUMBER: PREV200100285372
TITLE: **Tao** protein kinases and methods of use therefor.
AUTHOR(S): Cobb, Melanie (1); Hutchison, Michele; Chen, Zhu; Berman, Kevin
CORPORATE SOURCE: (1) Dallas, TX USA
ASSIGNEE: Board of Regents, University of Texas System
PATENT INFORMATION: US 6165461 December 26, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 26, 2000) Vol. 1241, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Compositions and methods are provided for potentiating the activity of the mitogen-activated protein kinase p38. In particular the mitogen-activated protein kinase kinase **MEK6**, and variants thereof that stimulate phosphorylation of p38 are provided. Such compounds may be used, for example, for therapy of diseases associated with the p38 cascade and to identify antibodies and other agents that inhibit or activate signal transduction via p38.

L4 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:605424 HCAPLUS
DOCUMENT NUMBER: 131:253126
TITLE: Molecular cloning and characterization of the mammalian Ste20-related kinases, PAK2 and **TAO1**
AUTHOR(S): Hutchison, Michele Rebecca
CORPORATE SOURCE: Southwestern Medical Center, Univ. of Texas, Dallas, TX, USA
SOURCE: (1999) No pp., Given Avail.: UMI, Order No. DA0800026 From: Diss. Abstr. Int., B 1999, 60(4), 1438
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L4 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:673061 HCAPLUS
DOCUMENT NUMBER: 131:318588
TITLE: **MEK**-phosphorylating **TAO** protein kinases and cDNAs and methods for drug screening and disease treatment
INVENTOR(S): Cobb, Melanie; Hutchison, Michele; Chen, Zhu; Berman,

Kevin
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9953076	A1	19991021	WO 1999-US8165	19990414
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6165461	A	20001226	US 1998-60410	19980414
CA 2325824	AA	19991021	CA 1999-2325824	19990414
AU 9935605	A1	19991101	AU 1999-35605	19990414
BR 9909679	A	20001219	BR 1999-9679	19990414
EP 1071787	A1	20010131	EP 1999-917495	19990414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002515223	T2	20020528	JP 2000-543623	19990414

PRIORITY APPLN. INFO.: US 1998-60410 A 19980414
WO 1999-US8165 W 19990414

AB Compns. and methods for modulating the activity of a MAP/ERK kinase, esp. **MEK3**, are disclosed. Thus, the cDNAs for two rat **MEK3** -phosphorylating protein kinases, **TAO1** and **TAO2**, were cloned and sequenced. These DNAs were used to identify ESTs encoding a human homolog of **TAO** kinase. In Northern blot anal., hybridization signals were strongest in both rat and human brain. In vivo, **TAO1** phosphorylated **MEK3** and copurified with it.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 9 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999428563 MEDLINE
DOCUMENT NUMBER: 99428563 PubMed ID: 10497253
TITLE: Isolation of the protein kinase **TAO2** and identification of its mitogen-activated protein kinase/extracellular signal-regulated kinase kinase binding domain.
AUTHOR: Chen Z; Hutchison M; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Oct 1) 274 (40) 28803-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF140556
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111

Last Updated on STN: 20000111
Entered Medline: 19991102

AB We previously reported the cloning of the thousand and one-amino acid protein kinase 1 (**TAO1**), a rat homolog of the Saccharomyces cerevisiae protein kinase sterile 20 protein. Here we report the complete sequence and properties of a related rat protein kinase **TAO2**. Like **TAO1**, recombinant **TAO2** selectively activated mitogen-activated protein/extracellular signal-regulated kinase kinases (**MEKs**) 3, 4, and 6 of the stress-responsive mitogen-activated protein kinase pathways in vitro and copurified with **MEK3** endogenous to Sf9 cells. To examine **TAO2** interactions with **MEKs**, the **MEK** binding domain of **TAO2** was localized to an approximately 135-residue sequence just C-terminal to the **TAO2** catalytic domain. In vitro this **MEK** binding domain associated with **MEKs** 3 and 6 but not **MEKs** 1, 2, or 4. Using chimeric **MEK** proteins, we found that the **MEK** N terminus was sufficient for binding to **TAO2**. Catalytic activity of full-length **TAO2** enhanced its binding to **MEKs**. However, neither the autophosphorylation of the **MEK** binding domain of **TAO2** nor the activity of **MEK** itself was required for **MEK** binding. These results suggest that **TAO** proteins lie in stress-sensitive kinase cascades and define a mechanism by which these kinases may organize downstream targets.

L4 ANSWER 8 OF 9 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999003202 MEDLINE
DOCUMENT NUMBER: 99003202 PubMed ID: 9786855
TITLE: Isolation of **TAO1**, a protein kinase that activates **MEKs** in stress-activated protein kinase cascades.
AUTHOR: Hutchison M; Berman K S; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: DK34128 (NIDDK)
GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 30) 273 (44) 28625-32.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF084205
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000606
Entered Medline: 19981201

AB Several components of the budding yeast pheromone-response pathway are conserved in mammalian mitogen-activated protein (MAP) kinase pathways. Thus, we used degenerate oligonucleotides derived from the sequence of the Saccharomyces cerevisiae protein kinase Ste20p to amplify related sequences from the rat. One of these sequences was used to clone a rat Ste20p homolog, which we called **TAO1** for its one thousand and one amino acids. Northern analysis shows **TAO1** is highly expressed in brain, as is a homolog **TAO2**. Recombinant **TAO1** was expressed and purified from Sf9 cells. In vitro, it activated MAP/extracellular signal-regulated protein kinase (ERK) kinases (**MEKs**) 3, 4, and 6 of the stress-responsive MAP kinase pathways, but not **MEK1** or 2 of the classical MAP kinase pathway. **TAO1** activated **MEK3** but not **MEK4** or **MEK6** in transfected cells. **MEK3** coimmunoprecipitated with **TAO1** when they were expressed in 293 cells. In addition,

immunoreactive **MEK3** endogenous to Sf9 cells copurified with **TAO1** produced from a recombinant baculovirus. The activation of and binding to **MEK3** by **TAO1** implicates **TAO1** in the regulation of the p38-containing stress-responsive MAP kinase pathway.

L4 ANSWER 9 OF 9 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999038267 MEDLINE
DOCUMENT NUMBER: 99038267 PubMed ID: 9820741
TITLE: The **TAO** of **MEKK**.
AUTHOR: Schlesinger T K; Fanger G R; Yujiri T; Johnson G L
CORPORATE SOURCE: Program in Molecular Signal Transduction, Division of Basic Sciences, National Jewish Medical and Research Center, 1400 Jackson St. Denver, CO 80206, USA.
CONTRACT NUMBER: DK 37871 (NIDDK)
DK 48845 (NIDDK)
GM 30324 (NIGMS)
+
SOURCE: FRONTIERS IN BIOSCIENCE, (1998 Nov 15) 3 D1181-6. Ref: 50
Journal code: 9702166. ISSN: 1093-4715.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20020420
Entered Medline: 19981209

AB Cloning and characterization of **MEKK1** in 1993 revealed that in addition to Raf there were other pathways activated by extracellular stimuli that were responsible for ERK activation. Since then, three additional **MEKK** family members have been cloned adding even further diversity to the regulation of MAPK pathways. The **MEKK** family members are regulated by a diverse array of extracellular stimuli ranging from growth factors to DNA damaging stimuli and so are important for the cell to sense exposure to various environmental stimuli. One important aspect of **MEKK** biology is that they can potentially serve in more than one pathway. Regulation of **MEKK** family members often involves LMWG proteins, phosphorylation and subcellular localization. With regard to at least **MEKK1**, serine/threonine kinases such as NIK, GLK and HPK1 appear also to be important for regulation. Of the **MEKK** family members, the biological role of **MEKK1** is best characterized and studies have shown that **MEKK1** is important in mediating survival vs. apoptosis, possibly via its ability to regulate transcription factors, the expression of death receptors and their ligands. The biological roles of **MEKK2**, 3 and 4 are under investigation and undoubtedly homologous deletion of these **MEKK** family members will be invaluable at determining the biological functions of these **MEKKs**. At present, the **MEKK** family members are characterized as localized sensors that control cell responses at the level of gene expression, metabolism and the cytoskeleton

=> d his

(FILE 'HOME' ENTERED AT 10:36:41 ON 16 MAY 2003)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:39:00 ON 16 MAY 2003

```
L1          5251 S TAO##
L2         39224 S MEK##
L3            29 S L1 AND L2
L4             9 DUP REM L3 (20 DUPLICATES REMOVED)

=> s modulat? or activat?
   5 FILES SEARCHED...
L5      4622124 MODULAT? OR ACTIVAT?

=> s p38
L6        30356 P38

=> s ATF2
L7         1054 ATF2

=> s l1 and l6
L8            13 L1 AND L6

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9             5 DUP REM L8 (8 DUPLICATES REMOVED)

=> d 1-5 ibib ab

L9   ANSWER 1 OF 5     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:   2001341539     MEDLINE
DOCUMENT NUMBER:    21238279   PubMed ID: 11279118
TITLE:              Regulation of stress-responsive mitogen-activated protein
                    (MAP) kinase pathways by TAO2.
AUTHOR:             Chen Z; Cobb M H
CORPORATE SOURCE:   Department of Pharmacology, University of Texas
                    Southwestern Medical Center, Dallas, Texas 75390-9041, USA.
CONTRACT NUMBER:    GM53032 (NIGMS)
SOURCE:             JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 May 11) 276 (19)
                    16070-5.
                    Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200106
ENTRY DATE:         Entered STN: 20010618
                    Last Updated on STN: 20030105
                    Entered Medline: 20010614
AB   Previous studies demonstrated that in vitro the protein kinase
     TAO2 activates MAP/ERK kinases (MEKs) 3, 4, and 6 toward their
     substrates p38 MAP kinase and c-Jun N-terminal
     kinase/stress-activated protein kinase (JNK/SAPK). In this study, we
     examined the ability of TAO2 to activate stress-sensitive MAP
     kinase pathways in cells and the relationship between activation of
     TAO2 and potential downstream pathways. Over-expression of
     TAO2 activated endogenous JNK/SAPK and p38 but not
     ERK1/2. Cotransfection experiments suggested that TAO2
     selectively activates MEK3 and MEK6 but not MEKs 1, 4, or 7.
     Coimmunoprecipitation demonstrated that endogenous TAO2
     specifically associates with MEK3 and MEK6 providing one mechanism for
     preferential recognition of MEKs upstream of p38. Sorbitol, and
     to a lesser extent, sodium chloride, Taxol, and nocodazole increased
     TAO2 activity toward itself and kinase-dead MEKs 3 and 6.
     Activation of endogenous TAO2 during differentiation of C2C12
     myoblasts paralleled activation of p38 but not JNK/SAPK,
     consistent with the idea that TAO2 is a physiological regulator
```

of **p38** under certain circumstances.

L9 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:285372 BIOSIS
DOCUMENT NUMBER: PREV200100285372
TITLE: **Tao** protein kinases and methods of use therefor.
AUTHOR(S): Cobb, Melanie (1); Hutchison, Michele; Chen, Zhu; Berman, Kevin
CORPORATE SOURCE: (1) Dallas, TX USA
ASSIGNEE: Board of Regents, University of Texas System
PATENT INFORMATION: US 6165461 December 26, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 26, 2000) Vol. 1241, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Compositions and methods are provided for potentiating the activity of the mitogen-activated protein kinase **p38**. In particular the mitogen-activated protein kinase kinase MEK6, and variants thereof that stimulate phosphorylation of **p38** are provided. Such compounds may be used, for example, for therapy of diseases associated with the **p38** cascade and to identify antibodies and other agents that inhibit or activate signal transduction via **p38**.

L9 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:355201 BIOSIS
DOCUMENT NUMBER: PREV200100355201
TITLE: **TAO** proteins mediate activation of the **p38** MAP kinase by Galphao and the subsequent activation of the downstream transcription factors.
AUTHOR(S): Chen, Zhu (1); Chen, Linda T. (1); Gilman, Alfred G. (1); Cobb, Melanie H.
CORPORATE SOURCE: (1) UT Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX, 75390 USA
SOURCE: Molecular Biology of the Cell, (Dec., 2000) Vol. 11, No. Supplement, pp. 31a. print.
Meeting Info.: 40th American Society for Cell Biology Annual Meeting San Francisco, CA, USA December 09-13, 2000
ISSN: 1059-1524.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L9 ANSWER 4 OF 5 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2001:123904 SCISEARCH
THE GENUINE ARTICLE: 377QY
TITLE: **TAO** proteins mediate activation of the **p38** MAP kinase by G alpha o and the subsequent activation of the downstream transcription factors
AUTHOR: Chen Z (Reprint); Chen L T; Gilman A G; Cobb M H
CORPORATE SOURCE: Univ Texas, SW Med Ctr, Dallas, TX 75390 USA
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (DEC 2000) Vol. 11, Supp. [S], pp. 31A-31A. MA 161.
Publisher: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.
ISSN: 1059-1524.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L9 ANSWER 5 OF 5 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999003202 MEDLINE
DOCUMENT NUMBER: 99003202 PubMed ID: 9786855
TITLE: Isolation of **TAO1**, a protein kinase that activates MEKs in stress-activated protein kinase cascades.
AUTHOR: Hutchison M; Berman K S; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: DK34128 (NIDDK)
GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 30) 273 (44) 28625-32.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF084205
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000606
Entered Medline: 19981201

AB Several components of the budding yeast pheromone-response pathway are conserved in mammalian mitogen-activated protein (MAP) kinase pathways. Thus, we used degenerate oligonucleotides derived from the sequence of the Saccharomyces cerevisiae protein kinase Ste20p to amplify related sequences from the rat. One of these sequences was used to clone a rat Ste20p homolog, which we called **TAO1** for its one thousand and one amino acids. Northern analysis shows **TAO1** is highly expressed in brain, as is a homolog **TAO2**. Recombinant **TAO1** was expressed and purified from Sf9 cells. In vitro, it activated MAP/extracellular signal-regulated protein kinase (ERK) kinases (MEKs) 3, 4, and 6 of the stress-responsive MAP kinase pathways, but not MEK1 or 2 of the classical MAP kinase pathway. **TAO1** activated MEK3 but not MEK4 or MEK6 in transfected cells. MEK3 coimmunoprecipitated with **TAO1** when they were expressed in 293 cells. In addition, immunoreactive MEK3 endogenous to Sf9 cells copurified with **TAO1** produced from a recombinant baculovirus. The activation of and binding to MEK3 by **TAO1** implicates **TAO1** in the regulation of the **p38**-containing stress-responsive MAP kinase pathway.

=> d his

(FILE 'HOME' ENTERED AT 10:36:41 ON 16 MAY 2003)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:39:00 ON 16 MAY 2003

```
L1          5251 S TAO##
L2         39224 S MEK##
L3            29 S L1 AND L2
L4             9 DUP REM L3 (20 DUPLICATES REMOVED)
L5       4622124 S MODULAT? OR ACTIVAT?
L6         30356 S P38
L7          1054 S ATF2
L8            13 S L1 AND L6
L9             5 DUP REM L8 (8 DUPLICATES REMOVED)
```

=> s l2 and l6
L10 4232 L2 AND L6

=> s l10 and l5

L11 4154 L10 AND L5

=> s s l11 and l7
MISSING OPERATOR S L11
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l11 and l7
L12 68 L11 AND L7

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13 20 DUP REM L12 (48 DUPLICATES REMOVED)

=> d 1-20 ibib ab

L13 ANSWER 1 OF 20 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2003081525 MEDLINE
DOCUMENT NUMBER: 22480177 PubMed ID: 12592382
TITLE: ERK signaling pathway is involved in p15INK4b/p16INK4a expression and HepG2 growth inhibition triggered by TPA and Saikosaponin a.
AUTHOR: Wen-Sheng Wu
CORPORATE SOURCE: Department of Medical Technology, TZU CHI University, Hualien, Taiwan.. wuws@mail.tcu.edu.tw
SOURCE: ONCOGENE, (2003 Feb 20) 22 (7) 955-63.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030221
Last Updated on STN: 20030316
Entered Medline: 20030314

AB The signal pathway mediating induction of p15(INK4b) and p16(INK4a) during HepG2 growth inhibition triggered by the phorbol ester tumor promoter TPA (12-O-tetradecanoylphorbol 13-acetate) and the Chinese herb Saikosaponin a was investigated. Western blot of three **activated** forms of mitogen-**activated** protein kinase (MAPK) (p-ERK, p-JNK and p-**p38**) demonstrated that phosphorylation of ERK is dramatically induced (11.6-fold) by TPA during 15 min to 1 h and significantly induced (2.5-fold) by Saikosaponin alpha at 30 min, whereas phosphorylation of JNK was induced only by TPA during 30 min to 1 h. Phosphorylation of **p38** was not induced by either drug. During this period, phosphorylation of one of the downstream transcriptional factors of MAPK cascade, **ATF2**, was 3.2- and 2.0-fold induced by TPA and Saikosaponin a, respectively, whereas that of another transcriptional factor, c-jun, was induced by TPA only. On the other hand, expressions of proto-oncogene c-jun, junB and c-fos were induced by TPA and Saikosaponin a during 30 min to 6 h of treatment. Pretreatment of 20 microg/ml PD98059, an inhibitor of **MEK** which is the upstream kinase of ERK, prevents the TPA- and Saikosaponin a-triggered HepG2 growth inhibition by 50 and 30%, respectively, accompanied by a 50 - 85% decrease of the p15(INK4b)/p16(INK4a) RNAs and proteins induced by both drugs. Inductions of c-fos RNA by both drugs and c-jun phosphorylation by TPA were also significantly reduced by PD98059 pretreatment. In addition, AP-1 DNA-binding assay using nonisotopic capillary electrophoresis and laser-induced fluorescence (CE/LIF) demonstrated that the AP-1-related DNA-binding activity was significantly induced by TPA and Saikosaponin a, which can be reduced by PD98059 pretreatment. These results suggested that **activation** of ERK together with its downstream

transcriptional machinery mediated p15(INK4b) and p16(INK4a) expression that led to HepG2 growth inhibition.

L13 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:142907 HCAPLUS
DOCUMENT NUMBER: 136:194260
TITLE: Methods for **modulating** multiple lineage kinase proteins and screening compounds which **modulate** multiple linease kinase proteins
INVENTOR(S): Maroney, Anna; Walton, Kevin M.; Dionne, Craig A.; Neff, Nicola; Knight, Ernest, Jr.; Glicksman, Marcie A.
PATENT ASSIGNEE(S): Cephalon, Inc., USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014536	A2	20020221	WO 2001-US24822	20010808
WO 2002014536	A3	20030130		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001083179	A5	20020225	AU 2001-83179	20010808
EP 1309721	A2	20030514	EP 2001-961958	20010808
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-637054 A 20000811
WO 2001-US24822 W 20010808
OTHER SOURCE(S): MARPAT 136:194260
AB Methods for identifying compds. which **modulate** activity of a multiple linease kinase protein and promotes cell survival or cell death comprising the steps of contacting the cell contg. the multiple linease protein with the compd., detg. whether the compd. decreases activity of the multiple linease protein, and detg. whether the compd. promotes cell survival are provided. Methods for identifying compds. which may be useful in the treatment of neurodegenerative disorders and/or inflammation are also provided. Methods for **modulating** the activity of a multiple linage kinase protein comprising contacting the protein or a cell contg. the protein with an indeno- or indolo-compd. of the invention are also provided. Methods of treating neurodegenerative disorders and/or inflammation are also provided.

L13 ANSWER 3 OF 20 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002413971 MEDLINE
DOCUMENT NUMBER: 22105769 PubMed ID: 12110590
TITLE: Growth factors can **activate ATF2** via a two-step mechanism: phosphorylation of Thr71 through the Ras-**MEK**-ERK pathway and of Thr69 through RalGDS-Src-**p38**.
AUTHOR: Ouwens D Margriet; de Ruiter Nancy D; van der Zon Gerard C M; Carter Andrew P; Schouten Jan; van der Burgt Corina;

Kooistra Klaas; Bos Johannes L; Maassen J Antonie; van Dam Hans

CORPORATE SOURCE: Department of Molecular Cell Biology, Section of Signal Transduction, Leiden University Medical Centre, Wassenaarseweg 72, 2333 AL Leiden, The Netherlands.

SOURCE: EMBO JOURNAL, (2002 Jul 15) 21 (14) 3782-93.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020810
Last Updated on STN: 20021015
Entered Medline: 20020905

AB Transcription factor **ATF2** regulates gene expression in response to environmental changes. Upon exposure to cellular stresses, the mitogen-**activated** proteinkinase (MAPK) cascades including SAPK/JNK and **p38** can enhance **ATF2**'s transactivating function through phosphorylation of Thr69 and Thr71. How ever, the mechanism of **ATF2 activation** by growth factors that are poor **activators** of JNK and **p38** is still elusive. Here, we show that in fibroblasts, insulin, epidermal growth factor (EGF) and serum **activate ATF2** via a so far unknown two-step mechanism involving two distinct Ras effector pathways: the Raf-**MEK**-ERK pathway induces phosphorylation of **ATF2** Thr71, whereas subsequent **ATF2** Thr69 phosphorylation requires the Ral-RalGDS-Src-**p38** pathway. Cooperation between ERK and **p38** was found to be essential for **ATF2** **activation** by these mitogens; the activity of **p38** and JNK/SAPK in growth factor-stimulated fibroblasts is insufficient to phosphorylate **ATF2** Thr71 or Thr69 + 71 significantly by themselves, while ERK cannot dual phosphorylate **ATF2** Thr69 + 71 efficiently. These results reveal a so far unknown mechanism by which distinct MAPK pathways and Ras effector pathways cooperate to **activate** a transcription factor.

L13 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:791398 HCAPLUS
DOCUMENT NUMBER: 138:89119

TITLE: Dietary salt intake **activates** MAP kinases in the rat kidney

AUTHOR(S): Ying, Wei-Zhong; Sanders, Paul W.

CORPORATE SOURCE: Nephrology Research and Training Center, Comprehensive Cancer Center, and Cell Adhesion and Matrix Research Center, Division of Nephrology, Department of Medicine, and Department of Physiology and Biophysics, University of Alabama at Birmingham, Birmingham, AL, 35294-0007, USA

SOURCE: FASEB Journal (2002), 16(12), 1683-1684, 10.1096/fj.01-0794fje
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study explored the hypothesis that dietary salt promoted changes in renal expression of TGF-.beta.1 and NOS3 by **modulating** the mitogen-**activated** protein kinase (MAPK) pathways. Sprague-Dawley rats were maintained for four days on formulated diets that contained 0.3, 1.0, 3.0, or 8.0% NaCl. An increase in salt intake to .gtoreq.3.0% NaCl increased kinase activities of **p38** MAPK and

p42/44 MAPK, but not p46/54 JNK/SAPK, in the cortex and outer and inner medulla. Assocd. with this increased activity was a relative increase in the phosphorylated forms of the transcription factors ATF-2 and Elk-1. Compared with rats on 0.3% NaCl diet, glomerular prepns. from rats on 8.0% NaCl diet contained more NOS3 and produced greater amts. of total and active TGF-.beta.1 and NOx. PD-098059, a **MEK1** inhibitor, and SB-203580, an inhibitor of **p38** MAPK.alpha.-.gamma., diminished NOS3 expression and prodn. of TGF-.beta.1 and NOx. TEA, administered i.v. 5 min before harvesting kidneys of rats on the 8.0% NaCl diet, decreased activities of both **p38** MAPK and p42/44 MAPK, compared with vehicle-treated animals. Thus, an increase in dietary salt **activated** through a TEA-sensitive pathway the **p38** MAPK and p42/44 MAPK signaling cascades, which promoted the increase in glomerular TGF-.beta.1 and NOS3 expression.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 20 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001276221 MEDLINE
DOCUMENT NUMBER: 21264641 PubMed ID: 11278744
TITLE: The **p38** MAPK pathway is required for cell growth inhibition of human breast cancer cells in response to activin.
AUTHOR: Cocolakis E; Lemay S; Ali S; Lebrun J J
CORPORATE SOURCE: Department of Medicine, Royal Victoria Hospital, Molecular Endocrinology Laboratory, McGill University, Montreal H3A 1A1, Canada.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 May 25) 276 (21) 18430-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20030105
Entered Medline: 20010705

AB Activin, a member of the TGFbeta family inhibits cell growth in various target tissues. Activin interacts with a complex of two receptors that upon **activation** phosphorylate specific intracellular mediators, the Smad proteins. The **activated** Smads interact with diverse DNA binding proteins and co-**activators** of transcription in a cell-specific manner, thus leading to various activin biological effects. In this study, we investigated the role and mechanism of action of activin in the human breast cancer T47D cells. We found that activin treatment of T47D cells leads to a dramatic decrease in cell growth. Thus activin appears as a potent cell growth inhibitor of these breast cancer cells. We show that activin induces the Smad pathway in these cells but also **activates** the **p38**-mitogen-**activated** protein kinase pathway, further leading to phosphorylation of the transcription factor **ATF2**. Finally, specific inhibitors of the **p38** kinase (SB202190, SB203580, and PD169316) but not an inactive analogue (SB202474) or the **MEK**-1 inhibitor PD98059 completely abolish the activin-mediated cell growth inhibition of T47D cells. Together, these results define a new role for activin in human breast cancer T47D cells and highlight a new pathway utilized by this growth factor in the mediation of its biological effects in cell growth arrest.

L13 ANSWER 6 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:594614 BIOSIS
DOCUMENT NUMBER: PREV200200594614

TITLE: Ras and Ral-dependent phosphorylation of **ATF2** mediates **activation** of the c-jun promoter by insulin.
AUTHOR(S): Ouwens, D. M. (1); van der Zon, G. C. M. (1); Maassen, J. A. (1); van Dam, H. (1)
CORPORATE SOURCE: (1) Leiden University Medical Centre, Leiden Netherlands
SOURCE: Diabetologia, (August, 2001) Vol. 44, No. Supplement 1, pp. A 27. print.
Meeting Info.: 37th Annual Meeting of the European Association for the Study of Diabetes Glasgow, Scotland, UK September 09-13, 2001 European Association for the Study of Diabetes
. ISSN: 0012-186X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L13 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:161543 HCAPLUS
DOCUMENT NUMBER: 132:217150
TITLE: Methods for identification of compounds **modulating** multiple lineage kinase proteins, compound preparation, and therapeutic use
INVENTOR(S): Maroney, Anna; Walton, Kevin M.; Dionne, Craig A.; Neff, Nicola; Knight, Ernest, Jr.; Glicksman, Marcie A.
PATENT ASSIGNEE(S): Cephalon, Inc., USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000013015	A1	20000309	WO 1999-US18864	19990818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2339539	AA	20000309	CA 1999-2339539	19990818
AU 9956793	A1	20000321	AU 1999-56793	19990818
EP 1105728	A1	20010613	EP 1999-943759	19990818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9913190	A	20011211	BR 1999-13190	19990818
JP 2002523780	T2	20020730	JP 2000-567949	19990818
NO 2001000389	A	20010402	NO 2001-389	20010123
BG 105360	A	20011031	BG 2001-105360	20010319
PRIORITY APPLN. INFO.:			US 1998-97980P P	19980826
			WO 1999-US18864 W	19990818

OTHER SOURCE(S): MARPAT 132:217150
AB Methods for identifying compds. which **modulate** activity of a multiple lineage kinase protein and promotes cell survival or cell death comprise contacting the cell contg. the multiple lineage kinase protein with the compd., detg. whether the compd. decreases activity of the multiple lineage kinase protein, and detg. whether the compd. promotes

cell survival are provided. Methods for identifying compds. which may be useful in the treatment of neurodegenerative disorders and/or inflammation are also provided. Methods for **modulating** the activity of a multiple lineage kinase protein comprising contacting the protein or a cell contg. the protein with an indeno- or indolo- compd. of the invention are also provided. Methods of treating neurodegenerative disorders and/or inflammation are also provided.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 20 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000287566 MEDLINE
DOCUMENT NUMBER: 20287566 PubMed ID: 10747925
TITLE: Signaling pathways to the assembly of an interferon-beta enhanceosome. Chemical genetic studies with a small molecule.
AUTHOR: Kim T; Kim T Y; Lee W G; Yim J; Kim T K
CORPORATE SOURCE: National Creative Research Initiative Center for Genetic Reprogramming, Institute for Molecular Biology and Genetics, Seoul National University, Seoul 151-742, Korea.. tk_kim@hms.harvard.edu
CONTRACT NUMBER: CA78048 (NCI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Jun 2) 275 (22) 16910-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000720
Last Updated on STN: 20020420
Entered Medline: 20000711

AB Small molecules that **modulate** specific protein functions are valuable tools for dissecting complex signaling pathways. Here, we identified a small molecule that induces the assembly of the interferon-beta (IFN-beta) enhanceosome by stimulating all the enhancer-binding **activator** proteins: **ATF2**/c-JUN, IRF3, and p50/p65 of NF-kappaB. This compound stimulates mitogen-**activated** protein kinase kinase kinase 1 (**MEKK1**), which is a member of a family of proteins involved in stress-mediated signaling pathways. Consistent with this, **MEKK1 activates** IRF3 in addition to **ATF2**/c-JUN and NF-kappaB for the assembly of the IFN-beta enhanceosome. **MEKK1 activates** IRF3 through the c-JUN amino-terminal kinase (JNK) pathway but not the **p38** and IkappaB kinase (IKK) pathway. Taken together with previous observations, these results implicate that, for the assembly of an IFN-beta enhanceosome, **MEKK1** can induce IRF3 and **ATF2** /c-JUN through the JNK pathway, whereas it can induce NF-kappaB through the IKK pathway. Thus, specific **MEKK** family proteins may be able to integrate some of multiple signal transduction pathways leading to the specific **activation** of the IFN-beta enhanceosome.

L13 ANSWER 9 OF 20 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2000239899 MEDLINE
DOCUMENT NUMBER: 20239899 PubMed ID: 10777545
TITLE: Stability of the **ATF2** transcription factor is regulated by phosphorylation and dephosphorylation.
AUTHOR: Fuchs S Y; Tappin I; Ronai Z
CORPORATE SOURCE: Ruttenberg Cancer Center, Mount Sinai School of Medicine, New York, New York 10029, USA.
CONTRACT NUMBER: CA59908 (NCI)

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Apr 28) 275 (17) 12560-4.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20021015
Entered Medline: 20000602

AB Trans-**activation** of the **activating** transcription factor-2 (**ATF2**) in response to cellular stress requires the N-terminal phosphorylation of **ATF2** by stress-**activated** protein kinases (SAPK). In this study, we investigated the role of **ATF2** phosphorylation in the maintenance of **ATF2** stability. **Activation** of SAPK by forced expression of DeltaMEKK1 increased overall **ATF2** ubiquitination, presumably because of the enhanced dimerization of **ATF2**. Treatment of DeltaMEKK1-expressing cells with okadaic acid led to the increase in N-terminal phosphorylation, protection from ubiquitination, and accumulation of exogenously expressed **ATF2**, indicating the role of protein phosphatases in balancing the effects of stress kinases. Analysis of ubiquitination and degradation of the constitutively dimerized **ATF2** mutant (**ATF2**(Delta150-248)) showed that **activation** of JNK or **p38** kinase renders **ATF2** resistant to ubiquitination and degradation. This effect is mediated by JNK/**p38**-dependent phosphorylation of **ATF2** at Thr-69 and Thr-71, because the phosphorylation-deficient mutant (**ATF2** (Delta150-248-T69A,T71A)) was not protected from ubiquitination and degradation by the **activation** of SAPK. Treatment of cells with okadaic acid elevated the tumor necrosis factor alpha-induced **ATF2** level and the extent of its specific N-terminal phosphorylation. Cycloheximide, which **activates** SAPK, while inhibiting protein synthesis, stabilized endogenous **ATF2**. However, treatment of cells with the high dose of SB203580, which inhibits JNK and **p38** kinase, resulted in efficient degradation of **ATF2** in cells exposed to cycloheximide. This degradation was abrogated by co-treatment with the proteasome inhibitor MG132. Our findings suggest that N-terminal phosphorylation of **ATF2** dimers protect **ATF2** from ubiquitination and degradation. We propose the hypothesis that the balance between SAPK and protein phosphatases affects the duration and magnitude of **ATF2** transcriptional output because of the effect on substrate recognition for ubiquitination and degradation.

L13 ANSWER 10 OF 20 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 6
ACCESSION NUMBER: 2000183668 EMBASE
TITLE: Contribution of MAP kinase pathways to the **activation** of ATF-2 in human neuroblastoma cells.
AUTHOR: Tindberg N.; Porsmyr-Palmertz M.; Simi A.
CORPORATE SOURCE: Dr. N. Tindberg, Division of Molecular Toxicology, IMM, Karolinska Instituter, S-171 77 Stockholm, Sweden. nictin@ki.se
SOURCE: Neurochemical Research, (2000) 25/4 (527-531).
Refs: 21
ISSN: 0364-3190 CODEN: NEREDZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Activated** Transcription Factor-2 (ATF-2) is important during development of and during injury to the brain. Both Jun N-terminal Kinases (JNKs) and **p38** Mitogen-**Activated** Protein Kinases (p38MAPKs) may phosphorylate ATF-2, but the contribution of these two pathways in cells has never been investigated. We have assayed endogenous p38MAPK activity in SK-N-MC and SH-SY5Y human neuroblastoma cells for **activation** of a GAL4/ATF-2 fusionprotein, by means of titrations of transfected expression plasmids and by using the p38MAPK inhibitor SB203580. It was found that basal **activation** of ATF-2 was independent of p38MAPK and that whereas MAPK kinase-3 (MKK3) was a weak inducer of ATF-2 **activation**, it was a potent **activator** of the stress **activated** transcription factor CHOP. In contrast, ATF-2 was very potently **activated** by the JNK pathway **activator** MAPK kinase kinase-1 (**MEKK1**). Thus, kinases downstream of **MEKK1** appear relevant, but it is unlikely that p38MAPKs contribute quantitatively to **activation** of **ATF2** in these cells.

L13 ANSWER 11 OF 20 MEDLINE
ACCESSION NUMBER: 1999436338 MEDLINE
DOCUMENT NUMBER: 99436338 PubMed ID: 10504489
TITLE: Role of MAP kinase pathways in mediating IL-6 production in human primary mesangial and proximal tubular cells.
AUTHOR: Leonard M; Ryan M P; Watson A J; Schramek H; Healy E
CORPORATE SOURCE: Department of Pharmacology, University College Dublin, Ireland.
SOURCE: KIDNEY INTERNATIONAL, (1999 Oct) 56 (4) 1366-77. Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991202

AB BACKGROUND: Both interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha) are pleiotropic cytokines that have been implicated in the development of glomerular and tubular injury in various forms of immune-mediated renal disease, including glomerulonephritis. Although TNF-alpha has been shown to stimulate IL-6 production in renal cells in culture, the signaling mechanisms that regulate IL-6 production are not fully understood. The aim of this study was to examine the role of the **p38** and extracellular signal-regulated kinase (ERK) mitogen-**activated** protein kinase (MAPK) pathways in regulating TNF-alpha-mediated IL-6 production from both primary human mesangial cells (HMCs) and human proximal tubular (HPT) cells. METHODS: Primary mesangial and proximal tubular cells were prepared from nephrectomized human kidney tissue. Cells were treated for 24 hours with TNF-alpha in the presence and absence of the specific **p38** and ERK1,2 MAPK inhibitors SB203580 and PD98059, respectively, either alone or in combination. IL-6 levels in the cell culture media were measured by enzyme-linked immunosorbent assay. MAPK **activation** was demonstrated by immunoblot for the active kinase (tyrosine/threonine phosphorylated) in whole cell extracts using phospho-specific antibodies. **p38** MAPK activity in HPT cells was measured using an in vitro immunokinase assay using **ATF2** as the substrate. RESULTS: TNF-alpha (0.1 to 100 ng/ml) stimulated a dose-dependent increase in IL-6 production in both renal cell types. The **activation** of the **p38** and the ERK1,2 MAPKs occurred following TNF-alpha stimulation. The role of these **activations** in IL-6 production was confirmed by the ability of both inhibitors SB203580 (1 to 30 microM) and PD98059 (0.01 to 10 microM)

to inhibit basal and TNF-alpha-stimulated IL-6 production in both cell types. The addition of both inhibitors in combination caused greater decreases in IL-6 production compared with either inhibitor alone. Pretreatment with SB203580 (10 microM) had no effect on basal or TNF-alpha-stimulated phosphorylation of **p38** MAPK but completely abolished TNF-alpha-stimulated **p38** MAPK activity. PD98059 decreased both basal and TNF-alpha-stimulated phosphorylation of ERK1,2. CONCLUSIONS: This study provides evidence that both the **p38** and ERK MAPK pathways are important for the regulation of the production of IL-6 from the proximal tubular and glomerular mesangial regions of the nephron. In response to TNF-alpha, the **activation** of both pathways leads to IL-6 production. These findings could aid in an understanding of the cellular mechanisms that regulate IL-6 production and could provide insights into possible pharmacological strategies in inflammatory renal disease.

L13 ANSWER 12 OF 20 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1998326314 MEDLINE
DOCUMENT NUMBER: 98326314 PubMed ID: 9661668
TITLE: Molecular cloning and characterization of a human protein kinase that specifically **activates** c-Jun N-terminal kinase.
AUTHOR: Yang J; New L; Jiang Y; Han J; Su B
CORPORATE SOURCE: Department of Immunology, University of Texas M. D. Anderson Cancer Center, Houston 77030, USA.
CONTRACT NUMBER: CA16672 (NCI)
SOURCE: GENE, (1998 May 28) 212 (1) 95-102.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF022805
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980811
Last Updated on STN: 20000606
Entered Medline: 19980727

AB The c-Jun N-terminal kinases (JNKs), also called stress-**activated** protein kinases (SAPKs), belong to the mitogen-**activated** protein kinase (MAPK) gene super-family. Like all the MAPKs, JNKs are **activated** through dual phosphorylation of a theronine residue and a tyrosine residue by a dual specificity kinase such as JNKK1/MKK4/SEK1. Here, we report the molecular cloning and characterization of hJNKK2 alpha, a human homolog of the recently reported murine MKK7 alpha. hJNKK2 alpha belongs to the MAPK kinase gene family and is expressed in many adult tissues. It is nearly identical to a recently reported human JNKK2 at the kinase domain but with major differences in both amino- and carboxyl-terminal sequences, suggesting that hJNKK2 alpha may be an alternative spliced form of this kinase. Expression of hJNKK2 alpha, but not its related kinases JNKK1/MKK4/SEK1, **MEK1**, MKK3, or MKK6, leads to strong **activation** of JNK in several cell lines. No **activation** of ERK or **p38** kinases was observed with this kinase. An in-vitro kinase assay demonstrated that JNK1 **activation** by hJNKK2 alpha requires phosphorylation of the theronine and tyrosine residues at positions 183 and 185 in JNK1. Furthermore, hJNKK2 alpha **activated** the JNK-dependent signal transduction pathway in vivo by induction of c-Jun- and **ATF2** -mediated gene transcription. In conclusion, we have cloned the human homolog of murine MKK7 alpha, which may be an alternative spliced form of human JNKK2 involved in transducing specific upstream signals to regulate JNK activity in vivo.

L13 ANSWER 13 OF 20 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 97382284 MEDLINE
DOCUMENT NUMBER: 97382284 PubMed ID: 9235954
TITLE: **p38**-2, a novel mitogen-**activated** protein kinase with distinct properties.
AUTHOR: Stein B; Yang M X; Young D B; Janknecht R; Hunter T; Murray B W; Barbosa M S
CORPORATE SOURCE: Signal Pharmaceuticals Inc., San Diego, California 92121, USA.. bstein@signalpharm.com
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Aug 1) 272 (31) 19509-17.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U92268
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970902
Last Updated on STN: 20021015
Entered Medline: 19970821

AB Mitogen-**activated** protein (MAP) kinases are involved in many cellular processes. Here we describe the cloning and characterization of a new MAP kinase, **p38**-2. **p38**-2 belongs to the **p38** subfamily of MAP kinases and shares with it the TGY phosphorylation motif. The complete **p38**-2 cDNA was isolated by polymerase chain reaction. It encodes a 364-amino acid protein with 73% identity to **p38**. Two shorter isoforms missing the phosphorylation motif were identified. Analysis of various tissues demonstrated that **p38**-2 is differently expressed from **p38**. Highest expression levels were found in heart and skeletal muscle. Like **p38**, **p38**-2 is **activated** by stress-inducing signals and proinflammatory cytokines. The preferred upstream kinase is **MEK6**. Although **p38**-2 and **p38** phosphorylate the same substrates, the site specificity of phosphorylation can differ as shown by two-dimensional phosphopeptide analysis of Sap-1a. Additionally, kinetic studies showed that **p38**-2 appears to be about 180 times more active than **p38** on certain substrates such as **ATF2**. Both kinases are inhibited by a class of pyridinyl imidazoles. **p38**-2 phosphorylation of **ATF2** and Sap-1a but not Elk1 results in increased transcriptional activity of these factors. A sequential kinetic mechanism of **p38**-2 is suggested by steady state kinetic analysis. In conclusion, **p38**-2 may be an important component of the stress response required for the homeostasis of a cell.

L13 ANSWER 14 OF 20 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 97294735 MEDLINE
DOCUMENT NUMBER: 97294735 PubMed ID: 9148940
TITLE: Cdc42Hs, but not Rac1, inhibits serum-stimulated cell cycle progression at G1/S through a mechanism requiring **p38**/RK.
AUTHOR: Molnar A; Theodoras A M; Zon L I; Kyriakis J M
CORPORATE SOURCE: Diabetes Research Laboratory, Massachusetts General Hospital East, Charlestown, Massachusetts 02129, USA.
CONTRACT NUMBER: DK41513 (NIDDK)
GM53697 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 May 16) 272 (20) 13229-35.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970630
Last Updated on STN: 20000303
Entered Medline: 19970619

AB Antimitogenic stimuli such as environmental or genotoxic stress, transforming growth factor-beta, and the inflammatory cytokines tumor necrosis factor and interleukin-1 **activate** two extracellular signal-regulated kinase (ERK)-based signaling pathways: the stress-**activated** protein kinase (SAPK/JNK) pathway and the **p38** pathway. **Activated p38** phosphorylates transcription factors important in the regulation of cell growth and apoptosis, including **activating** transcription factor 2 (**ATF2**), Max, cAMP response element-binding protein-homologous protein/growth arrest DNA damage 153 (CHDP/GADD153). In turn, **p38** lies downstream of the Rho family GTPases Cdc42Hs and Rac1, as well as at least three mitogen-**activated** protein kinase (MAPK)/ERK-kinases (**MEKs**): MAPK kinases-3, -6, and SAPK/ERK-kinase-1. Although many of the stimuli that **activate p38** can also inhibit cell cycle progression, a clear-cut role for the **p38** pathway in cell cycle regulation has not been established. Using a quantitative microinjection approach, we show here that Cdc42Hs, but not Rac1 or RhoA, can inhibit cell cycle progression at G1/S through a mechanism requiring **activation** of **p38**. These results suggest a novel role for Cdc42Hs in cell cycle inhibition. Furthermore, these results suggest that although both Cdc42Hs and Rac1 can **activate p38** in situ, the effects of Cdc42Hs and Rac1 on cell cycle progression are, in fact, quite distinct.

L13 ANSWER 15 OF 20 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 97:497887 SCISEARCH
THE GENUINE ARTICLE: XG520
TITLE: **Activation** of the novel stress-**activated** protein kinase SAPK4 by cytokines and cellular stresses is mediated by SKK3 (MKK6); Comparison of its substrate specificity with that of other SAP kinases
AUTHOR: Goedert M (Reprint); Cuenda A; Craxton M; Jakes R; Cohen P
CORPORATE SOURCE: MRC, MOL BIOL LAB, HILLS RD, CAMBRIDGE CB2 2QH, ENGLAND (Reprint); UNIV DUNDEE, DEPT BIOCHEM, MRC, PROT PHOSPHORYLAT UNIT, DUNDEE DD1 4HN, SCOTLAND
COUNTRY OF AUTHOR: ENGLAND; SCOTLAND
SOURCE: EMBO JOURNAL, (16 JUN 1997) Vol. 16, No. 12, pp. 3563-3571
.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD, ENGLAND OX2 6DP.
ISSN: 0261-4189.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 49

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A cDNA was cloned that encodes human stress-**activated** protein kinase-4 (SAPK4), a novel MAP kinase family member whose amino acid sequence is similar to 60% identical to that of the other three SAP kinases which contain a TGY motif in their **activation** domain. The mRNA encoding SAPK4 was found to be widely distributed in human tissues. When expressed in KB cells, SAPK4 was **activated** in response to cellular stresses and pro-inflammatory cytokines, in a manner similar to other SAPKs. SAPK4 was **activated** in vitro by SKK3 (also called MKK6) or when co-transfected with SKK3 into COS cells. SKK3 was the only **activator** of SAPK4 that was induced when KB cells

were exposed to a cellular stress or stimulated with interleukin-1. These findings indicate that SKK3 mediates the **activation** of SAPK4. The substrate specificity of SAPK4 in vitro was similar to that of SAPK3. Both enzymes phosphorylated the transcription factors **ATF2**, Elk-1 and SAP-1 at similar rates, but were far less effective than SAPK2a (also called RK/**p38**) or SAPK2b (also called **p38** beta) in **activating** MAPKAP kinase-2 and MAPKAP kinase-3. Unlike SAPK1 (also called JNK), SAPK3 and SAPK4 did not phosphorylate the **activation** domain of c-Jun. Unlike SAPK2a and SAPK2b, SAPK4 and SAPK3 were not inhibited by the drugs SB 203580 and SB 202190. Our results suggest that cellular functions previously attributed to SAPK1 and/or SAPK2 may be mediated by SAPK3 or SAPK4.

L13 ANSWER 16 OF 20 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 97:116666 SCISEARCH
THE GENUINE ARTICLE: WF380
TITLE: **Activation** of stress-**activated** protein kinase-3 (SAPK3) by cytokines and cellular stresses is mediated via SAPKK3 (MKK6); Comparison of the specificities of SAPK3 and SAPK2 (RK/**p38**)
AUTHOR: Cuenda A; Cohen P (Reprint); BueeScherrer V; Goedert M
CORPORATE SOURCE: UNIV DUNDEE, DEPT BIOCHEM, MRC, PROT PHOSPHORYLAT UNIT, DUNDEE DD1 4HN, SCOTLAND (Reprint); UNIV DUNDEE, DEPT BIOCHEM, MRC, PROT PHOSPHORYLAT UNIT, DUNDEE DD1 4HN, SCOTLAND
COUNTRY OF AUTHOR: SCOTLAND
SOURCE: EMBO JOURNAL, (15 JAN 1997) Vol. 16, No. 2, pp. 295-305. Publisher: OXFORD UNIV PRESS UNITED KINGDOM, WALTON ST JOURNALS DEPT, OXFORD, ENGLAND OX2 6DP. ISSN: 0261-4189.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 61

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Stress-**activated** protein kinase-3 (SAPK3), a recently described MAP kinase family member with a widespread tissue distribution, was transfected into several mammalian cell lines and shown to be **activated** in response to cellular stresses, interleukin-1 (IL-1) and tumour necrosis factor (TNF) in a similar manner to SAPK1 (also termed JNK) and SAPK2 (also termed **p38**, RK, CSBP and Mxi2), SAPK3 and SAPK2 were **activated** at similar rates in vitro by SAPKK3 (also termed MKK6), and SAPKK3 was the only **activator** of SAPK3 that was induced when KB or 293 cells were exposed to cellular stresses or stimulated with IL-1 or TNF, Co-transfection with SAPKK3 induced SAPK3 activity and greatly enhanced **activation** in response to osmotic shock, These experiments indicate that SAPKK3 mediates the **activation** of SAPK3 in several mammalian cells, SAPK3 and SAPK2 phosphorylated a number of proteins at similar rates, including the transcription factors **ATF2**, Elk-1 and SAP1, but SAPK3 was far less effective than SAPK2 in **activating** MAPKAP kinase-2 and MAPKAP kinase-3. Unlike SAPK2, SAPK3 was not inhibited by the drug SE 203580, SAPK3 phosphorylated **ATF2** at Thr69, Thr71 and Ser90, the same residues phosphorylated by SAPK1, whereas SAPK2 only phosphorylated Thr69 and Thr71, Our results suggest that cellular functions previously attributed to SAPK1 and/or SAPK2 may be mediated by SAPK3.

L13 ANSWER 17 OF 20 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 96212215 MEDLINE
DOCUMENT NUMBER: 96212215 PubMed ID: 8626699
TITLE: Cloning and characterization of **MEK6**, a novel member of the mitogen-**activated** protein kinase

kinase cascade.
AUTHOR: Stein B; Brady H; Yang M X; Young D B; Barbosa M S
CORPORATE SOURCE: Signal Pharmaceuticals Inc., San Diego, California 92121, USA.. bstein@signalpharm.com
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 May 10) 271 (19) 11427-33.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U10871; GENBANK-U49732
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 20000303
Entered Medline: 19960627

AB Mitogen-**activated** protein kinases are members of a conserved cascade of kinases involved in many signal transduction pathways. They stimulate phosphorylation of transcription factors in response to extracellular signals such as growth factors, cytokines, ultraviolet light, and stress-inducing agents. A novel mitogen-**activated** protein kinase kinase, **MEK6**, was cloned and characterized. The complete **MEK6** cDNA was isolated by polymerase chain reaction. It encodes a 334-amino acid protein with 82% identity to MKK3. **MEK6** is highly expressed in skeletal muscle like many other members of this family, but in contrast to MKK3 its expression in leukocytes is very low. **MEK6** is a member of the **p38** kinase cascade and efficiently phosphorylates **p38** but not c-Jun N-terminal kinase (JNK) and extracellular signal-regulated kinase (ERK) family members in direct kinase assays. Coupled kinase assays demonstrated that **MEK6** induces phosphorylation of **ATF2** by **p38** but does not phosphorylate **ATF2** directly. **MEK6** is strongly **activated** by UV, anisomycin, and osmotic shock but not by phorbol esters, nerve growth factor, and epidermal growth factor. This separates **MEK6** from the ERK subgroup of protein kinases. **MEK6** is only a poor substrate for **MEKK**, a mitogen-**activated** protein kinase kinase kinase that efficiently phosphorylates the related family member JNKK.

L13 ANSWER 18 OF 20 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 96:732646 SCISEARCH
THE GENUINE ARTICLE: VL333
TITLE: REGULATION OF MITOGEN-**ACTIVATED** PROTEIN-KINASES BY A CALCIUM/CALMODULIN-DEPENDENT PROTEIN-KINASE CASCADE
AUTHOR: ENSLEN H; TOKUMITSU H; STORK P J S; DAVIS R J; SODERLING T R (Reprint)
CORPORATE SOURCE: OREGON HLTH SCI UNIV, VOLLUM INST, 3181 SW SAM JACKSON PK RD, PORTLAND, OR, 97201 (Reprint); OREGON HLTH SCI UNIV, VOLLUM INST, PORTLAND, OR, 97201; UNIV MASSACHUSETTS, SCH MED, HOWARD HUGHES MED INST, WORCESTER, MA, 01605; UNIV MASSACHUSETTS, SCH MED, PROGRAM MOL MED, WORCESTER, MA, 01605
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (01 OCT 1996) Vol. 93, No. 20, pp. 10803-10808.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 59
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Membrane depolarization of NG108 cells gives rapid (<5 min) **activation** of Ca2+/calmodulin-dependent protein kinase IV (CaM-KIV), as well as **activation** of c-Jun N-terminal kinase (JNK), To investigate whether the Ca2+-dependent **activation** of mitogen-**activated** protein kinases (ERK, JNK, and **p38**) might be mediated by the CaM kinase cascade, we have transfected PC12 cells, which lack CaM-KIV, with constitutively active mutants of CaM kinase kinase and/or CaM-KIV (CaM-KKc and CaM-KIVc, respectively), In the absence of depolarization, CaM-KK, transfection had no effect on Elk-dependent transcription of a luciferase reporter gene, whereas CaM-KIVc alone or in combination with CaM-KKc gave 7- to 10-fold and 60- to 80-fold stimulations, respectively, which were blocked by mitogen-**activated** protein (MAP) kinase phosphatase cotransfection. When epitope-tagged constructs of MAP kinases were cotransfected with CaM-KKc plus CaM-KIVc, the immunoprecipitated MAP kinases were **activated** 2-fold (ERK-2) and 7- to 10-fold (JNK-1 and **p38**), The JNK and **p38** pathways were further investigated using specific c-Jun or **ATF2**-dependent transcriptional assays, We found that c-Jun/**ATF2**-dependent transcriptions were enhanced 7- to 10-fold by CaM-KIVc and 20- to 30-fold by CaM-KKc plus CaM-KIVc. In the case of the Jun-dependent transcription, this effect was not due to direct phosphorylation of c-Jun by **activated** CaM-KIV, since transcription was blocked by a dominant-negative JNK and by two MAP kinase phosphatases, Mutation of the phosphorylation site (Thr(196)) in CaM-KIV, which mediates its **activation** by CaM-KIV kinase, prevented **activation** of Elk-1, c-Jun, and **ATF2** by the CaM kinase cascade, These results establish a new Ca2+-dependent mechanism for regulating MAP kinase pathways and resultant transcription.

L13 ANSWER 19 OF 20 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 96305034 MEDLINE
DOCUMENT NUMBER: 96305034 PubMed ID: 8755992
TITLE: Stimulation of the stress-**activated** mitogen-**activated** protein kinase subfamilies in perfused heart. **p38**/RK mitogen-**activated** protein kinases and c-Jun N-terminal kinases are **activated** by ischemia/reperfusion.
AUTHOR: Bogoyevitch M A; Gillespie-Brown J; Ketterman A J; Fuller S J; Ben-Levy R; Ashworth A; Marshall C J; Sugden P H
CORPORATE SOURCE: National Heart and Lung Institute (Cardiac Medicine), Imperial College of Science, University of London, UK.
SOURCE: CIRCULATION RESEARCH, (1996 Aug) 79 (2) 162-73. Ref: 108
Journal code: 0047103. ISSN: 0009-7330.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 20020420
Entered Medline: 19961212

AB It has recently been recognized that cellular stresses **activate** certain members of the mitogen-**activated** protein kinase (MAPK) superfamily. One role of these "stress-**activated**" MAPKs is to increase the transactivating activity of the transcription factors c-Jun, Elk1, and **ATF2**. These findings may be particularly relevant to hearts that have been exposed to pathological stresses. Using the isolated perfused rat heart, we show that global ischemia does not **activate** the 42- and 44-kD extracellular signal-regulated (protein) kinase (ERK) subfamily of MAPKs but rather stimulates a 38-kD

activator of MAPK-**activated** protein kinase-2 (MAPKAPK2). This **activation** is maintained during reperfusion. The molecular characteristics of this protein kinase suggest that it is a member of the **p38**/reactivating kinase (RK) group of stress-**activated** MAPKs. In contrast, stress-**activated** MAPKs of the c-Jun N-terminal kinase (JNK/SAPKs) subfamily are not **activated** by ischemia alone but are **activated** by reperfusion following ischemia. Furthermore, transfection of ventricular myocytes with **activated** protein kinases (**MEKK1** and SEK1) that may be involved in the upstream **activation** of JNK/ SAPKs induces increases in myocyte size and transcriptional changes typical of the hypertrophic response. We speculate that **activation** of multiple parallel MAPK pathways may be important in the responses of hearts to cellular stresses.

L13 ANSWER 20 OF 20 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 95:842810 SCISEARCH
THE GENUINE ARTICLE: TH643
TITLE: TRANSCRIPTIONAL REGULATION BY MAP KINASES
AUTHOR: DAVIS R J (Reprint)
CORPORATE SOURCE: UNIV MASSACHUSETTS, MED CTR, SCH MED, DEPT BIOCHEM & MOLEC BIOL, PROGRAM MOLEC MED, WORCESTER, MA, 01605 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR REPRODUCTION AND DEVELOPMENT, (DEC 1995) Vol. 42, No. 4, pp. 459-467.
ISSN: 1040-452X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 31
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Tyrosine kinase growth factor receptors **activate** MAP kinase by a complex mechanism involving the SH2/3 protein Grb2, the exchange protein Sos, and Ras. The GTP-bound Pas protein binds to the Raf kinase and initiates a protein kinase cascade that leads to MAP kinase **activation**. Three MAP kinase kinase kinases have been described-c-Raf, c-Mos, and **Mekk**-that phosphorylate and **activate Mek**, the MAP kinase kinase. **Activated Mek** phosphorylates and **activates** MAP kinase. Subsequently, the **activated** MAP kinase translocates into the nucleus where many of the physiological targets of the MAP kinase signal transduction pathway are located. These substrates include transcription factors that are regulated by MAP kinase phosphorylation (e.g., Elk-1, c-Myc, c-Jun, c-Fos, and C/EBP beta). Thus the MAP kinase pathway represents a significant mechanism of signal transduction by growth factor receptors from the cell surface to the nucleus that results in the regulation of gene expression.

Three MAP kinase homologs have been identified in the rat: Erk1, Erk2, and Erk3. Human MAP kinases that are similar to the rat Erk kinases have also been identified by molecular cloning. The human Erk1 protein kinase has been shown to be widely expressed as a 44-kDa protein in many tissues. The human Erk2 protein kinase is a 41-kDa protein that is expressed ubiquitously. In contrast, a human Erk3-related protein kinase has been found to be expressed at a high level only in heart muscle and brain. The loci of these MAP kinase genes are widely distributed within the human genome: erk2 at 22q11.2; erk1 at 16p11.2; and ek3-related at 18q12-21.

In the yeast Saccharomyces cerevisiae, five MAP kinase gene homologs have been described: smk1, mpk1, hog1, fus3,and kss1. Together, these kinases are a more diverse group than the human erks that have been identified. Thus the erks are likely to represent only one subgroup of a larger human MAP kinase gene family. A candidate for this extended family of MAP kinases is the c-lun NH2-terminal kinase (Jnk), which binds to and

phosphorylates the transcription factor c-lun at the **activating** sites Ser-63 and Ser-73. Evidence is presented here to demonstrate that Jnk is a distant relative of the MAP kinase group that is **activated** by dual phosphorylation at Tyr and Thr. (C) 1995 Wiley-Liss, Inc.

```
=> d his

     (FILE 'HOME' ENTERED AT 10:36:41 ON 16 MAY 2003)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 10:39:00 ON 16 MAY 2003
L1          5251 S TAO##
L2         39224 S MEK##
L3            29 S L1 AND L2
L4             9 DUP REM L3 (20 DUPLICATES REMOVED)
L5       4622124 S MODULAT? OR ACTIVAT?
L6         30356 S P38
L7          1054 S ATF2
L8            13 S L1 AND L6
L9             5 DUP REM L8 (8 DUPLICATES REMOVED)
L10         4232 S L2 AND L6
L11         4154 S L10 AND L5
L12           68 S  L11 AND L7
L13           20 DUP REM L12 (48 DUPLICATES REMOVED)

=> e cobb m h/au
E1           13     COBB M E/AU
E2            4     COBB M G/AU
E3          572 --> COBB M H/AU
E4            2     COBB M H */AU
E5            5     COBB M J/AU
E6            1     COBB M K/AU
E7           38     COBB M L/AU
E8           44     COBB M M/AU
E9           10     COBB M N/AU
E10           1     COBB M R/AU
E11           1     COBB M S/AU
E12           1     COBB M V JR/AU

=> s e3
L14         572 "COBB M H"/AU

=> s l1 and l14
L15          15 L1 AND L14

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16           5 DUP REM L15 (10 DUPLICATES REMOVED)

=> d 1-5 ibib ab

L16  ANSWER 1 OF 5     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:    2001341539     MEDLINE
DOCUMENT NUMBER:     21238279   PubMed ID: 11279118
TITLE:               Regulation of stress-responsive mitogen-activated protein
                     (MAP) kinase pathways by TAO2.
AUTHOR:              Chen Z; Cobb M H
CORPORATE SOURCE:    Department of Pharmacology, University of Texas
                     Southwestern Medical Center, Dallas, Texas 75390-9041, USA.
CONTRACT NUMBER:     GM53032 (NIGMS)
```

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 May 11) 276 (19) 16070-5.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20030105
Entered Medline: 20010614

AB Previous studies demonstrated that in vitro the protein kinase **TAO2** activates MAP/ERK kinases (MEKs) 3, 4, and 6 toward their substrates p38 MAP kinase and c-Jun N-terminal kinase/stress-activated protein kinase (JNK/SAPK). In this study, we examined the ability of **TAO2** to activate stress-sensitive MAP kinase pathways in cells and the relationship between activation of **TAO2** and potential downstream pathways. Over-expression of **TAO2** activated endogenous JNK/SAPK and p38 but not ERK1/2. Cotransfection experiments suggested that **TAO2** selectively activates MEK3 and MEK6 but not MEKs 1, 4, or 7. Coimmunoprecipitation demonstrated that endogenous **TAO2** specifically associates with MEK3 and MEK6 providing one mechanism for preferential recognition of MEKs upstream of p38. Sorbitol, and to a lesser extent, sodium chloride, Taxol, and nocodazole increased **TAO2** activity toward itself and kinase-dead MEKs 3 and 6. Activation of endogenous **TAO2** during differentiation of C2C12 myoblasts paralleled activation of p38 but not JNK/SAPK, consistent with the idea that **TAO2** is a physiological regulator of p38 under certain circumstances.

L16 ANSWER 2 OF 5 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001687134 MEDLINE
DOCUMENT NUMBER: 21590367 PubMed ID: 11733138
TITLE: kin-18, a C. elegans protein kinase involved in feeding.
AUTHOR: Berman K S; Hutchison M; Avery L; **Cobb M H**
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX, USA.
CONTRACT NUMBER: GM53032 (NIGMS)
HL46154 (NHLBI)
SOURCE: GENE, (2001 Nov 28) 279 (2) 137-47.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011205
Last Updated on STN: 20020125
Entered Medline: 20020122

AB **TAO1** and **TAO2** are recently described protein kinases whose initial characterization has placed them at the mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK) kinase kinase (MEKK) level of stress-responsive MAPK pathways. Because their physiological roles have not been identified, we sought to study their C. elegans homolog to learn more about their functions. kin-18 encodes a previously uncharacterized protein in C. elegans whose catalytic domain shares over 60% identity with **TAO1** and **TAO2**. We demonstrate that KIN-18 is a protein of 120 kDa whose promoter is active in the pharynx and intestine of C. elegans. To learn more about **TAO**/KIN-18 function, we studied how expression of constitutively active forms of **TAO1** or KIN-18 would affect the physiology of

intact worms. Strains of C. elegans expressing active forms of **TAO1** or KIN-18 exhibit altered pharyngeal electrophysiology as measured by electropharyngeogram. These worms grow more slowly and lay fewer eggs, phenotypes that could result from reduced feeding. We have also identified a C. elegans gene that encodes a protein kinase similar to mammalian MAPK/ERK Kinase (MEK) 4 whose promoter is active in the pharynx. It is phosphorylated by **TAO1** in vitro and physically interacts with **TAO1**.

L16 ANSWER 3 OF 5 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2001:123904 SCISEARCH
THE GENUINE ARTICLE: 377QY
TITLE: **TAO** proteins mediate activation of the p38 MAP kinase by G alpha o and the subsequent activation of the downstream transcription factors
AUTHOR: Chen Z (Reprint); Chen L T; Gilman A G; **Cobb M H**
CORPORATE SOURCE: Univ Texas, SW Med Ctr, Dallas, TX 75390 USA
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (DEC 2000) Vol. 11, Supp. [S], pp. 31A-31A. MA 161.
Publisher: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.
ISSN: 1059-1524.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L16 ANSWER 4 OF 5 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999428563 MEDLINE
DOCUMENT NUMBER: 99428563 PubMed ID: 10497253
TITLE: Isolation of the protein kinase **TAO2** and identification of its mitogen-activated protein kinase/extracellular signal-regulated kinase kinase binding domain.
AUTHOR: Chen Z; Hutchison M; **Cobb M H**
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Oct 1) 274 (40) 28803-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF140556
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991102

AB We previously reported the cloning of the thousand and one-amino acid protein kinase 1 (**TAO1**), a rat homolog of the Saccharomyces cerevisiae protein kinase sterile 20 protein. Here we report the complete sequence and properties of a related rat protein kinase **TAO2**. Like **TAO1**, recombinant **TAO2** selectively activated mitogen-activated protein/extracellular signal-regulated kinase kinases (MEKs) 3, 4, and 6 of the stress-responsive mitogen-activated protein kinase pathways in vitro and copurified with MEK3 endogenous to Sf9 cells. To examine **TAO2** interactions with MEKs, the MEK binding domain of **TAO2** was localized to an approximately 135-residue sequence just C-terminal to the **TAO2** catalytic domain. In vitro this MEK binding domain associated with MEKs 3 and 6 but not MEKs 1, 2, or 4.

Using chimeric MEK proteins, we found that the MEK N terminus was sufficient for binding to **TAO2**. Catalytic activity of full-length **TAO2** enhanced its binding to MEKs. However, neither the autophosphorylation of the MEK binding domain of **TAO2** nor the activity of MEK itself was required for MEK binding. These results suggest that **TAO** proteins lie in stress-sensitive kinase cascades and define a mechanism by which these kinases may organize downstream targets.

L16 ANSWER 5 OF 5 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999003202 MEDLINE
DOCUMENT NUMBER: 99003202 PubMed ID: 9786855
TITLE: Isolation of **TAO1**, a protein kinase that activates MEKs in stress-activated protein kinase cascades.
AUTHOR: Hutchison M; Berman K S; **Cobb M H**
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: DK34128 (NIDDK)
GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 30) 273 (44) 28625-32.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF084205
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000606
Entered Medline: 19981201

AB Several components of the budding yeast pheromone-response pathway are conserved in mammalian mitogen-activated protein (MAP) kinase pathways. Thus, we used degenerate oligonucleotides derived from the sequence of the Saccharomyces cerevisiae protein kinase Ste20p to amplify related sequences from the rat. One of these sequences was used to clone a rat Ste20p homolog, which we called **TAO1** for its one thousand and one amino acids. Northern analysis shows **TAO1** is highly expressed in brain, as is a homolog **TAO2**. Recombinant **TAO1** was expressed and purified from Sf9 cells. In vitro, it activated MAP/extracellular signal-regulated protein kinase (ERK) kinases (MEKs) 3, 4, and 6 of the stress-responsive MAP kinase pathways, but not MEK1 or 2 of the classical MAP kinase pathway. **TAO1** activated MEK3 but not MEK4 or MEK6 in transfected cells. MEK3 coimmunoprecipitated with **TAO1** when they were expressed in 293 cells. In addition, immunoreactive MEK3 endogenous to Sf9 cells copurified with **TAO1** produced from a recombinant baculovirus. The activation of and binding to MEK3 by **TAO1** implicates **TAO1** in the regulation of the p38-containing stress-responsive MAP kinase pathway.

=> d his

(FILE 'HOME' ENTERED AT 10:36:41 ON 16 MAY 2003)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:39:00 ON 16 MAY 2003
L1 5251 S TAO##
L2 39224 S MEK##
L3 29 S L1 AND L2
L4 9 DUP REM L3 (20 DUPLICATES REMOVED)
L5 4622124 S MODULAT? OR ACTIVAT?

```
L6         30356 S P38
L7          1054 S ATF2
L8            13 S L1 AND L6
L9             5 DUP REM L8 (8 DUPLICATES REMOVED)
L10         4232 S L2 AND L6
L11         4154 S L10 AND L5
L12           68 S  L11 AND L7
L13           20 DUP REM L12 (48 DUPLICATES REMOVED)
                 E COBB M H/AU
L14          572 S E3
L15           15 S L1 AND L14
L16            5 DUP REM L15 (10 DUPLICATES REMOVED)

=> e hutchison m/au
E1             1     HUTCHISON LINNAE/AU
E2             2     HUTCHISON LISA C/AU
E3           158 --> HUTCHISON M/AU
E4             4     HUTCHISON M A/AU
E5             2     HUTCHISON M C/AU
E6             2     HUTCHISON M D/AU
E7            13     HUTCHISON M E/AU
E8             7     HUTCHISON M F/AU
E9             3     HUTCHISON M G/AU
E10           18     HUTCHISON M J/AU
E11            9     HUTCHISON M K/AU
E12           27     HUTCHISON M L/AU

=> s e3
L17          158 "HUTCHISON M"/AU

=> e chen z/au
E1             1     CHEN YYM/AU
E2             1     CHEN YZ/AU
E3          6923 --> CHEN Z/AU
E4            14     CHEN Z A/AU
E5             2     CHEN Z ANDY/AU
E6           157     CHEN Z B/AU
E7           430     CHEN Z C/AU
E8           335     CHEN Z D/AU
E9             1     CHEN Z DUAN/AU
E10            5     CHEN Z E/AU
E11          274     CHEN Z F/AU
E12          465     CHEN Z G/AU

=> s e3
L18         6923 "CHEN Z"/AU

=> e berman k s/au
E1             1     BERMAN K K/AU
E2             5     BERMAN K M/AU
E3            24 --> BERMAN K S/AU
E4             1     BERMAN K V/AU
E5             7     BERMAN KAREN/AU
E6            10     BERMAN KAREN F/AU
E7            40     BERMAN KAREN FAITH/AU
E8             1     BERMAN KARN FAITH/AU
E9             1     BERMAN KEITH E/AU
E10            2     BERMAN KENNETH/AU
E11            3     BERMAN KENNETH M/AU
E12           14     BERMAN KEVIN/AU

=> s e3
```

L19 24 "BERMAN K S"/AU

=> s l17-l19
L20 7093 (L17 OR L18 OR L19)

=> s l1 and l20
L21 15 L1 AND L20

=> dup rem l21
PROCESSING COMPLETED FOR L21
L22 5 DUP REM L21 (10 DUPLICATES REMOVED)

=> d 1-5 ibib ab

L22 ANSWER 1 OF 5 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001341539 MEDLINE
DOCUMENT NUMBER: 21238279 PubMed ID: 11279118
TITLE: Regulation of stress-responsive mitogen-activated protein (MAP) kinase pathways by **TAO2**.
AUTHOR: **Chen Z**; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75390-9041, USA.
CONTRACT NUMBER: GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 May 11) 276 (19) 16070-5.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20030105
Entered Medline: 20010614

AB Previous studies demonstrated that in vitro the protein kinase **TAO2** activates MAP/ERK kinases (MEKs) 3, 4, and 6 toward their substrates p38 MAP kinase and c-Jun N-terminal kinase/stress-activated protein kinase (JNK/SAPK). In this study, we examined the ability of **TAO2** to activate stress-sensitive MAP kinase pathways in cells and the relationship between activation of **TAO2** and potential downstream pathways. Over-expression of **TAO2** activated endogenous JNK/SAPK and p38 but not ERK1/2. Cotransfection experiments suggested that **TAO2** selectively activates MEK3 and MEK6 but not MEKs 1, 4, or 7. Coimmunoprecipitation demonstrated that endogenous **TAO2** specifically associates with MEK3 and MEK6 providing one mechanism for preferential recognition of MEKs upstream of p38. Sorbitol, and to a lesser extent, sodium chloride, Taxol, and nocodazole increased **TAO2** activity toward itself and kinase-dead MEKs 3 and 6. Activation of endogenous **TAO2** during differentiation of C2C12 myoblasts paralleled activation of p38 but not JNK/SAPK, consistent with the idea that **TAO2** is a physiological regulator of p38 under certain circumstances.

L22 ANSWER 2 OF 5 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001687134 MEDLINE
DOCUMENT NUMBER: 21590367 PubMed ID: 11733138
TITLE: kin-18, a C. elegans protein kinase involved in feeding.
AUTHOR: **Berman K S**; **Hutchison M**; Avery L; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX, USA.

CONTRACT NUMBER: GM53032 (NIGMS)
HL46154 (NHLBI)
SOURCE: GENE, (2001 Nov 28) 279 (2) 137-47.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011205
Last Updated on STN: 20020125
Entered Medline: 20020122

AB **TAO1** and **TAO2** are recently described protein kinases whose initial characterization has placed them at the mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK) kinase kinase (MEKK) level of stress-responsive MAPK pathways. Because their physiological roles have not been identified, we sought to study their C. elegans homolog to learn more about their functions. kin-18 encodes a previously uncharacterized protein in C. elegans whose catalytic domain shares over 60% identity with **TAO1** and **TAO2**. We demonstrate that KIN-18 is a protein of 120 kDa whose promoter is active in the pharynx and intestine of C. elegans. To learn more about **TAO**/KIN-18 function, we studied how expression of constitutively active forms of **TAO1** or KIN-18 would affect the physiology of intact worms. Strains of C. elegans expressing active forms of **TAO1** or KIN-18 exhibit altered pharyngeal electrophysiology as measured by electropharyngeogram. These worms grow more slowly and lay fewer eggs, phenotypes that could result from reduced feeding. We have also identified a C. elegans gene that encodes a protein kinase similar to mammalian MAPK/ERK Kinase (MEK) 4 whose promoter is active in the pharynx. It is phosphorylated by **TAO1** in vitro and physically interacts with **TAO1**.

L22 ANSWER 3 OF 5 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2001:123904 SCISEARCH
THE GENUINE ARTICLE: 377QY
TITLE: **TAO** proteins mediate activation of the p38 MAP kinase by G alpha o and the subsequent activation of the downstream transcription factors
AUTHOR: **Chen Z (Reprint)**; Chen L T; Gilman A G; Cobb M H
CORPORATE SOURCE: Univ Texas, SW Med Ctr, Dallas, TX 75390 USA
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (DEC 2000) Vol. 11, Supp. [S], pp. 31A-31A. MA 161.
Publisher: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.
ISSN: 1059-1524.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L22 ANSWER 4 OF 5 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999428563 MEDLINE
DOCUMENT NUMBER: 99428563 PubMed ID: 10497253
TITLE: Isolation of the protein kinase **TAO2** and identification of its mitogen-activated protein kinase/extracellular signal-regulated kinase kinase binding domain.
AUTHOR: **Chen Z; Hutchison M;** Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: GM53032 (NIGMS)

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Oct 1) 274 (40) 28803-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF140556
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991102

AB We previously reported the cloning of the thousand and one-amino acid protein kinase 1 (**TAO1**), a rat homolog of the Saccharomyces cerevisiae protein kinase sterile 20 protein. Here we report the complete sequence and properties of a related rat protein kinase **TAO2**. Like **TAO1**, recombinant **TAO2** selectively activated mitogen-activated protein/extracellular signal-regulated kinase kinases (MEKs) 3, 4, and 6 of the stress-responsive mitogen-activated protein kinase pathways in vitro and copurified with MEK3 endogenous to Sf9 cells. To examine **TAO2** interactions with MEKs, the MEK binding domain of **TAO2** was localized to an approximately 135-residue sequence just C-terminal to the **TAO2** catalytic domain. In vitro this MEK binding domain associated with MEKs 3 and 6 but not MEKs 1, 2, or 4. Using chimeric MEK proteins, we found that the MEK N terminus was sufficient for binding to **TAO2**. Catalytic activity of full-length **TAO2** enhanced its binding to MEKs. However, neither the autophosphorylation of the MEK binding domain of **TAO2** nor the activity of MEK itself was required for MEK binding. These results suggest that **TAO** proteins lie in stress-sensitive kinase cascades and define a mechanism by which these kinases may organize downstream targets.

L22 ANSWER 5 OF 5 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999003202 MEDLINE
DOCUMENT NUMBER: 99003202 PubMed ID: 9786855
TITLE: Isolation of **TAO1**, a protein kinase that activates MEKs in stress-activated protein kinase cascades.
AUTHOR: **Hutchison M; Berman K S;** Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: DK34128 (NIDDK)
GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 30) 273 (44) 28625-32.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF084205
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000606
Entered Medline: 19981201

AB Several components of the budding yeast pheromone-response pathway are conserved in mammalian mitogen-activated protein (MAP) kinase pathways. Thus, we used degenerate oligonucleotides derived from the sequence of the Saccharomyces cerevisiae protein kinase Ste20p to amplify related sequences from the rat. One of these sequences was used to clone a rat Ste20p homolog, which we called **TAO1** for its one thousand and one amino acids. Northern analysis shows **TAO1** is highly

expressed in brain, as is a homolog **TAO2**. Recombinant **TAO1** was expressed and purified from Sf9 cells. In vitro, it activated MAP/extracellular signal-regulated protein kinase (ERK) kinases (MEKs) 3, 4, and 6 of the stress-responsive MAP kinase pathways, but not MEK1 or 2 of the classical MAP kinase pathway. **TAO1** activated MEK3 but not MEK4 or MEK6 in transfected cells. MEK3 coimmunoprecipitated with **TAO1** when they were expressed in 293 cells. In addition, immunoreactive MEK3 endogenous to Sf9 cells copurified with **TAO1** produced from a recombinant baculovirus. The activation of and binding to MEK3 by **TAO1** implicates **TAO1** in the regulation of the p38-containing stress-responsive MAP kinase pathway.

=> d his

(FILE 'HOME' ENTERED AT 10:36:41 ON 16 MAY 2003)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:39:00 ON 16 MAY 2003

```
L1          5251 S TAO##
L2         39224 S MEK##
L3            29 S L1 AND L2
L4             9 DUP REM L3 (20 DUPLICATES REMOVED)
L5       4622124 S MODULAT? OR ACTIVAT?
L6         30356 S P38
L7          1054 S ATF2
L8            13 S L1 AND L6
L9             5 DUP REM L8 (8 DUPLICATES REMOVED)
L10         4232 S L2 AND L6
L11         4154 S L10 AND L5
L12           68 S  L11 AND L7
L13           20 DUP REM L12 (48 DUPLICATES REMOVED)
                 E COBB M H/AU
L14          572 S E3
L15           15 S L1 AND L14
L16            5 DUP REM L15 (10 DUPLICATES REMOVED)
                 E HUTCHISON M/AU
L17          158 S E3
                 E CHEN Z/AU
L18         6923 S E3
                 E BERMAN K S/AU
L19           24 S E3
L20         7093 S L17-L19
L21           15 S L1 AND L20
L22            5 DUP REM L21 (10 DUPLICATES REMOVED)
```

```
=> d his

     (FILE 'HOME' ENTERED AT 11:51:11 ON 16 MAY 2003)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 11:51:43 ON 16 MAY 2003
L1             3 S "CETAO"
L2         39224 S MEK##
L3             3 S CE"TAO##"
L4             0 S L2 AND L3
L5          5251 S TAO##
L6             2 S CE(A)L5
L7         22193 S "C. ELEGANS"
L8             8 S L5 AND L7
L9             6 S L8 AND L2
L10            1 DUP REM L9 (5 DUPLICATES REMOVED)

=
```

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1652MXM

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT

```
                MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
                AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS     STN Operating Hours Plus Help Desk Availability
 NEWS INTER     General Internet Information
 NEWS LOGIN     Welcome Banner and News Items
 NEWS PHONE     Direct Dial and Telecommunication Network Access to STN
 NEWS WWW       CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:51:11 ON 16 MAY 2003

=> d his

     (FILE 'HOME' ENTERED AT 11:51:11 ON 16 MAY 2003)

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 11:51:43 ON 16 MAY 2003

FILE 'EMBASE' ENTERED AT 11:51:43 ON 16 MAY 2003
COPYRIGHT (C) 2003 Elsevier Science B.V.  All rights reserved.

FILE 'BIOSIS' ENTERED AT 11:51:43 ON 16 MAY 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'BIOTECHDS' ENTERED AT 11:51:43 ON 16 MAY 2003
COPYRIGHT (C) 2003 THOMSON DERWENT AND INSTITUTE FOR SCIENTIFIC INFORMATION

FILE 'SCISEARCH' ENTERED AT 11:51:43 ON 16 MAY 2003
COPYRIGHT 2003 THOMSON ISI

FILE 'HCAPLUS' ENTERED AT 11:51:43 ON 16 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'NTIS' ENTERED AT 11:51:43 ON 16 MAY 2003
Compiled and distributed by the NTIS, U.S. Department of Commerce.
It contains copyrighted material.
All rights reserved. (2003)

FILE 'LIFESCI' ENTERED AT 11:51:43 ON 16 MAY 2003
COPYRIGHT (C) 2003 Cambridge Scientific Abstracts (CSA)


=> s "ceTAO"
L1            3 "CETAO"

=> s mek##
```

```
L2       39224 MEK##

=> s ce"tao##"
L3           3 CE"TAO##"

=> s l2 and l3
L4           0 L2 AND L3

=> d l1 1-3 ibib ab

L1     ANSWER 1 OF 3     NTIS COPYRIGHT 2003 NTIS
ACCESSION NUMBER:        1978(42):04197
NTIS ORDER NUMBER:       PB-285 026/1/XAB
TITLE:                   Phase Relationships and Crystal Chemistry of Compounds
                         Containing Cerium Oxide. Final rept.
AUTHOR:                  Roth, R. S.; Negas, T.; Parker, H. S.; Minor, D. B.;
                         Olson, C. D.
CORPORATE SOURCE:        National Bureau of Standards, Washington, D.C. (240800)
NUMBER OF REPORT:        PB-285 026/1/XAB
                         9p; 1978
CONTROLLED TERM:         Report
COUNTRY:                 United States
LANGUAGE:                English
AVAILABILITY:            Pub. in Proceedings Rare Earth Research Conf. (13th),
                         Held at Olgebay, West Virginia on October 16-20, 1977.
                         Paper in The Rare Earths in Modern Science and
                         Technology, p163-171 1978.
                         NTIS Prices: Not available NTIS
OTHER SOURCE:            GRA&I7825
AB       The crystal chemistry and oxidation-reduction behavior of CeTaO
         (4+x) and CeNbO(4+x) suggest that ceramics based on these materials
         could be exploited as electrodes in high temperature applications.
         However, these systems are so complex that useful materials could be
         developed only after considerable modification and control of chemical
         features. Nevertheless, the Ce(+3) = Ce(+4) couple offers promise for
         electronic conduction in cerium oxide-based phases provided that a
         suitable host structure can be found. This paper reviews the efforts
         underway to develop such a host material from systems containing rare
         earth oxides, niobium and tantalum oxides and Fe2O3.

L1     ANSWER 2 OF 3     NTIS COPYRIGHT 2003 NTIS
ACCESSION NUMBER:        1978(42):02069
NTIS ORDER NUMBER:       PB-284 595/6/XAB
TITLE:                   Crystal Chemistry and Oxidation-Reduction of Phases in
                         Rare Earth Tantalate-Niobate Systems. Final rept.
AUTHOR:                  Cava, R. J.; Negas, T.; Roth, R. S.; Parker, H. S.;
                         Minor, D. B.
CORPORATE SOURCE:        National Bureau of Standards, Washington, D.C. (240800)
NUMBER OF REPORT:        PB-284 595/6/XAB
                         7p; 1978
CONTROLLED TERM:         Report
COUNTRY:                 United States
LANGUAGE:                English
AVAILABILITY:            Pub. in Proceedings Rare Earth Research Conference
                         (13th), Held at Olgebay, West Virginia on October
                         16-20, 1977. Paper in The Rare Earths in Modern Science
                         and Technology, p181-187 1978.
                         NTIS Prices: Not available NTIS
OTHER SOURCE:            GRA&I7824
AB       The data on crystal chemistry and oxidation-reduction phenomena of
         CeTaO(4+x) and CeNbO(4+x) have been extended. Phase transition
         temperatures were determined by high temperature x-ray diffraction for
```

LaTaO4, CeTaO4, and PrTaO4 and for solid solutions of PrTaO4-NdTaO4. The oxidation/reduction behavior of **CeTaO**(4+x) and CeNbO(4+x) was studied.

L1 ANSWER 3 OF 3 NTIS COPYRIGHT 2003 NTIS
ACCESSION NUMBER: 1978(38):04860
NTIS ORDER NUMBER: PB-278 404/9/XAB
TITLE: Crystal Chemistry of Cerium Titanates, Tantalates and Niobates. Final rept.
Reprint: Crystal Chemistry of Cerium Titanates, Tantalates and Niobates.
AUTHOR: Roth, R. S.; Negas, T.; Parker, H. S.; Minor, D. B.; Jones, C.
CORPORATE SOURCE: National Bureau of Standards, Washington, D.C. (240800)
NUMBER OF REPORT: PB-278 404/9/XAB
10p; 1977
CONTROLLED TERM: Report
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: Pub. in Materials Research Bulletin 12, p1173-1182 1977.
NTIS Prices: Not available NTIS
OTHER SOURCE: GRA&I7811
AB Cerium dioxide has been found to react with other oxides at high temperatures in an open air environment with the formation of Ce(+3), Ce(+4) or mixed valence phases. Single crystals of Ce(+3)Ta7O19 reveal that this compound is hexagonal. Another phase which is also light yellow is formed by oxidizing at 350C for long periods of time and corresponds to **CeTaO**(4.50).

```
=> d his

     (FILE 'HOME' ENTERED AT 11:51:11 ON 16 MAY 2003)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 11:51:43 ON 16 MAY 2003
L1             3 S "CETAO"
L2         39224 S MEK##
L3             3 S CE"TAO##"
L4             0 S L2 AND L3

=> s tao##
L5          5251 TAO##

=> s ce(a)l5
L6             2 CE(A) L5

=> d 1-2 ibib ab
```

L6 ANSWER 1 OF 2 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1998:802231 SCISEARCH
THE GENUINE ARTICLE: 128CG
TITLE: Reversible Oxidation/Reduction in the CeTaO4+delta system: a TEM and XRD study
AUTHOR: Drew G; Withers R L (Reprint); Larsson A K; Schmid S
CORPORATE SOURCE: AUSTRALIAN NATL UNIV, RES SCH CHEM, GPO BOX 4, CANBERRA, ACT 0200, AUSTRALIA (Reprint); AUSTRALIAN NATL UNIV, RES SCH CHEM, CANBERRA, ACT 0200, AUSTRALIA
COUNTRY OF AUTHOR: AUSTRALIA
SOURCE: JOURNAL OF SOLID STATE CHEMISTRY, (OCT 1998) Vol. 140, No. 1, pp. 20-28.

Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 0022-4596.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 8

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A detailed TEM and XRD study has been made of the basic crystallography (unit cells, space group symmetries, and min relationships) of each of the three oxidized phases which occur in the CeTaO4 + delta system, their structural relationship to stoichiometric **Ce**+ (**TaO4**)-Ta-III, and their temperature-dependent redox reactions. Such crystallographic knowledge is essential to understand the structural relationships between the various phases and to gain insight into the oxidation/reduction mechanisms allowing the formation of the oxidized phases. Twinning is found to be endemic in stoichiometric **Ce**+ (**TaO4**)-Ta-III as well as in each of the oxidized Series 2, 3, and 4 phases; the twin plane relating the twin variants is derived in each case. (C) 1998 Academic Press.

L6 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1983:544870 HCAPLUS
DOCUMENT NUMBER: 99:144870
TITLE: Industrial Heat Treatment and Equipment for Silicate, Vol. 2: Industrial Heat Treatment Equipment for Ceramics (Qi Suan Yan Gong Ye Re Gong Guo Cheng ji She Bei (Xia **Ce Tao** Ci Gong Ye Re Gong She Bei))
CORPORATE SOURCE: South China College of Engineering, Peop. Rep. China; Ching Hua University
SOURCE: (1982) Publisher: (Chinese Jiangzhu Gongye Publ. House: Beijing, Peop. Rep. China), 191 pp. .yen.1.35.
DOCUMENT TYPE: Book
LANGUAGE: Chinese
AB Unavailable

```
=> s "c. elegans"
L7       22193 "C. ELEGANS"

=> d his

     (FILE 'HOME' ENTERED AT 11:51:11 ON 16 MAY 2003)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 11:51:43 ON 16 MAY 2003
L1             3 S "CETAO"
L2         39224 S MEK##
L3             3 S CE"TAO##"
L4             0 S L2 AND L3
L5          5251 S TAO##
L6             2 S CE(A)L5
L7         22193 S "C. ELEGANS"

=> s l5 and l7
L8             8 L5 AND L7

=> s l8 and l2
L9             6 L8 AND L2

=> dup rem l9
```

PROCESSING COMPLETED FOR L9
L10 1 DUP REM L9 (5 DUPLICATES REMOVED)

=> d ibib ab

L10 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001687134 MEDLINE
DOCUMENT NUMBER: 21590367 PubMed ID: 11733138
TITLE: kin-18, a **C. elegans** protein kinase involved in feeding.
AUTHOR: Berman K S; Hutchison M; Avery L; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX, USA.
CONTRACT NUMBER: GM53032 (NIGMS)
HL46154 (NHLBI)
SOURCE: GENE, (2001 Nov 28) 279 (2) 137-47.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011205
Last Updated on STN: 20020125
Entered Medline: 20020122

AB **TAO1** and **TAO2** are recently described protein kinases whose initial characterization has placed them at the mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK) kinase kinase (**MEKK**) level of stress-responsive MAPK pathways. Because their physiological roles have not been identified, we sought to study their **C. elegans** homolog to learn more about their functions. kin-18 encodes a previously uncharacterized protein in **C. elegans** whose catalytic domain shares over 60% identity with **TAO1** and **TAO2**. We demonstrate that KIN-18 is a protein of 120 kDa whose promoter is active in the pharynx and intestine of **C. elegans**. To learn more about **TAO**/KIN-18 function, we studied how expression of constitutively active forms of **TAO1** or KIN-18 would affect the physiology of intact worms. Strains of **C. elegans** expressing active forms of **TAO1** or KIN-18 exhibit altered pharyngeal electrophysiology as measured by electropharyngeogram. These worms grow more slowly and lay fewer eggs, phenotypes that could result from reduced feeding. We have also identified a **C. elegans** gene that encodes a protein kinase similar to mammalian MAPK/ERK Kinase (**MEK**) 4 whose promoter is active in the pharynx. It is phosphorylated by **TAO1** in vitro and physically interacts with **TAO1**.

=> d his

(FILE 'HOME' ENTERED AT 11:51:11 ON 16 MAY 2003)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 11:51:43 ON 16 MAY 2003
L1 3 S "CETAO"
L2 39224 S MEK##
L3 3 S CE"TAO##"
L4 0 S L2 AND L3
L5 5251 S TAO##
L6 2 S CE(A)L5

L7	22193	S "C. ELEGANS"
L8	8	S L5 AND L7
L9	6	S L8 AND L2
L10	1	DUP REM L9 (5 DUPLICATES REMOVED)

ACCESSION NUMBER: 1999428563 MEDLINE
DOCUMENT NUMBER: 99428563 PubMed ID: 10497253
TITLE: Isolation of the protein kinase **TAO2** and identification of its mitogen-activated protein kinase/extracellular signal-regulated kinase kinase binding domain.
AUTHOR: Chen Z; Hutchison M; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Oct 1) 274 (40) 28803-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF140556
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991102

AB We previously reported the cloning of the thousand and one-amino acid protein kinase 1 (**TAO1**), a rat homolog of the Saccharomyces cerevisiae protein kinase sterile 20 protein. Here we report the complete sequence and properties of a related rat protein kinase **TAO2**. Like **TAO1**, recombinant **TAO2** selectively activated mitogen-activated protein/extracellular signal-regulated kinase kinases (**MEKs**) 3, 4, and 6 of the stress-responsive mitogen-activated protein kinase pathways in vitro and copurified with **MEK3** endogenous to Sf9 cells. To examine **TAO2** interactions with **MEKs**, the **MEK** binding domain of **TAO2** was localized to an approximately 135-residue sequence just C-terminal to the **TAO2** catalytic domain. In vitro this **MEK** binding domain associated with **MEKs** 3 and 6 but not **MEKs** 1, 2, or 4. Using chimeric **MEK** proteins, we found that the **MEK** N terminus was sufficient for binding to **TAO2**. Catalytic activity of full-length **TAO2** enhanced its binding to **MEKs**. However, neither the autophosphorylation of the **MEK** binding domain of **TAO2** nor the activity of **MEK** itself was required for **MEK** binding. These results suggest that **TAO** proteins lie in stress-sensitive kinase cascades and define a mechanism by which these kinases may organize downstream targets.

L4 ANSWER 8 OF 9 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999003202 MEDLINE
DOCUMENT NUMBER: 99003202 PubMed ID: 9786855
TITLE: Isolation of **TAO1**, a protein kinase that activates **MEKs** in stress-activated protein kinase cascades.
AUTHOR: Hutchison M; Berman K S; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: DK34128 (NIDDK)
GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 30) 273

Thus, we used degenerate oligonucleotides derived from the sequence of the Saccharomyces cerevisiae protein kinase Ste20p to amplify related sequences from the rat. One of these sequences was used to clone a rat Ste20p homolog, which we called **TAO1** for its one thousand and one amino acids. Northern analysis shows **TAO1** is highly expressed in brain, as is a homolog **TAO2**. Recombinant **TAO1** was expressed and purified from Sf9 cells. In vitro, it activated MAP/extracellular signal-regulated protein kinase (ERK) kinases (MEKs) 3, 4, and 6 of the stress-responsive MAP kinase pathways, but not MEK1 or 2 of the classical MAP kinase pathway. **TAO1** activated MEK3 but not MEK4 or MEK6 in transfected cells. MEK3 coimmunoprecipitated with **TAO1** when they were expressed in 293 cells. In addition, immunoreactive MEK3 endogenous to Sf9 cells copurified with **TAO1** produced from a recombinant baculovirus. The activation of and binding to MEK3 by **TAO1** implicates **TAO1** in the regulation of the **p38**-containing stress-responsive MAP kinase pathway.

=>

L9 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:355201 BIOSIS
DOCUMENT NUMBER: PREV200100355201
TITLE: **TAO** proteins mediate activation of the **p38** MAP kinase by Galphao and the subsequent activation of the downstream transcription factors.
AUTHOR(S): Chen, Zhu (1); Chen, Linda T. (1); Gilman, Alfred G. (1); Cobb, Melanie H.
CORPORATE SOURCE: (1) UT Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX, 75390 USA
SOURCE: Molecular Biology of the Cell, (Dec., 2000) Vol. 11, No. Supplement, pp. 31a. print.
Meeting Info.: 40th American Society for Cell Biology Annual Meeting San Francisco, CA, USA December 09-13, 2000
ISSN: 1059-1524.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L9 ANSWER 4 OF 5 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2001:123904 SCISEARCH
THE GENUINE ARTICLE: 377QY
TITLE: **TAO** proteins mediate activation of the **p38** MAP kinase by G alpha o and the subsequent activation of the downstream transcription factors
AUTHOR: Chen Z (Reprint); Chen L T; Gilman A G; Cobb M H
CORPORATE SOURCE: Univ Texas, SW Med Ctr, Dallas, TX 75390 USA
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (DEC 2000) Vol. 11, Supp. [S], pp. 31A-31A. MA 161.
Publisher: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.
ISSN: 1059-1524.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L9 ANSWER 5 OF 5 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999003202 MEDLINE
DOCUMENT NUMBER: 99003202 PubMed ID: 9786855
TITLE: Isolation of **TAO1**, a protein kinase that activates MEKs in stress-activated protein kinase cascades.
AUTHOR: Hutchison M; Berman K S; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: DK34128 (NIDDK)
GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 30) 273 (44) 28625-32.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF084205
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000606
Entered Medline: 19981201
AB Several components of the budding yeast pheromone-response pathway are conserved in mammalian mitogen-activated protein (MAP) kinase pathways.

ACCESSION NUMBER: 1999003202 MEDLINE
DOCUMENT NUMBER: 99003202 PubMed ID: 9786855
TITLE: Isolation of **TAO1**, a protein kinase that activates **MEKs** in stress-activated protein kinase cascades.
AUTHOR: Hutchison M; Berman K S; Cobb M H
CORPORATE SOURCE: Department of Pharmacology, University of Texas Southwestern Medical Center, Dallas, Texas 75235-9041, USA.
CONTRACT NUMBER: DK34128 (NIDDK)
GM53032 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 30) 273 (44) 28625-32.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF084205
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000606
Entered Medline: 19981201
AB Several components of the budding yeast pheromone-response pathway are conserved in mammalian mitogen-activated protein (MAP) kinase pathways. Thus, we used degenerate oligonucleotides derived from the sequence of the Saccharomyces cerevisiae protein kinase Ste20p to amplify related sequences from the rat. One of these sequences was used to clone a rat Ste20p homolog, which we called **TAO1** for its one thousand and one amino acids. Northern analysis shows **TAO1** is highly expressed in brain, as is a homolog **TAO2**. Recombinant **TAO1** was expressed and purified from Sf9 cells. In vitro, it activated MAP/extracellular signal-regulated protein kinase (ERK) kinases (**MEKs**) 3, 4, and 6 of the stress-responsive MAP kinase pathways, but not **MEK1** or 2 of the classical MAP kinase pathway. **TAO1** activated **MEK3** but not **MEK4** or **MEK6** in transfected cells. **MEK3** coimmunoprecipitated with **TAO1** when they were expressed in 293 cells. In addition, immunoreactive **MEK3** endogenous to Sf9 cells copurified with **TAO1** produced from a recombinant baculovirus. The activation of and binding to **MEK3** by **TAO1** implicates **TAO1** in the regulation of the p38-containing stress-responsive MAP kinase